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7-Deoxy-L-manno-L-*gala*-heptose and Some of its Derivatives

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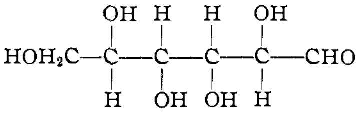
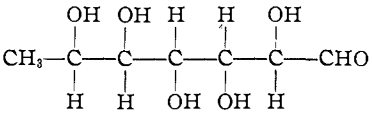
7-Deoxy-L-manno-L-*gala*-heptose has been crystallized as an α-form having initial $[\alpha]^{20}\mathrm{D}$ −128.6°. The sugar forms three crystalline methyl glycosides, which are shown to be methyl 7-deoxy-L-manno-α-L-*gala*-heptopyranoside, methyl 7-deoxy-L-manno-β-L-*gala*-heptopyranoside and methyl 7-deoxy-L-manno-β-L-*gala*-heptofuranoside. The tetraacetates of the three methyl glycosides, the α- and β-pentaacetates of the sugar, tetraacetyl-7-deoxy-L-manno-α-L-*gala*-heptosyl bromide and the corresponding chloride are described. Molecular rotations of the compounds in the 7-deoxy-L-manno-L-*gala*-heptose series are compared with rotations of the corresponding compounds in the D-galactose and D-manno-D-*gala*-heptose series.

7-Deoxy-L-manno-L-*gala*-heptose was prepared from L-rhamnose by Fischer and Piloty,[2] who named it *l*-α-rhamnohexose. The configuration of carbon atoms one to five is like that of L-galactose. The heptose crystallizes from water as an α-form having an extrapolated initial specific rotation in water of −128.6° and a final rotation of −62.5°. Fischer and Piloty[2] found $[\alpha]^{20}\mathrm{D}$ −82.9° (30 min.) and −61.4° (final). The sugar yields by the usual reaction with methanol containing hydrogen chloride three crystalline methyl glycosides, two of which consume two moles of periodate on a molar basis and accordingly are pyranosides. The third methyl glycoside consumed 5.7 moles of periodate during 23 hours at 26° and 5.9 moles during 43 hours. This result is consistent with the furanoside structure (I), since the initial oxidation product (II) is subject to further oxidation to produce III,[3] which would be oxidized to the glyoxylic acid ester (IV). This ester upon spontaneous hydrolysis yields products that react with two moles of periodate to make the total consumption six moles. A confirmation of the furanoside structure is found in the comparatively rapid rate of hydrolysis of this glycoside by acid, its rate being about fifteen times that of the pyranosides. It is designated a β-form (in the L-*gala* series) because of its large dextro rotation. The tetraacetates of the three methyl glycosides, also the α- and β-pentaacetates of the sugar, tetraacetyl-7-deoxy-L-manno-α-L-*gala*-heptosyl bromide and the corresponding chloride have been prepared. The specific and molecular rotations of these compounds and similar data reported by us in 1934[4,5] for 7-deoxy-L-manno-L-*gala*-heptonic lactone, the aldonic acid amide and phenylhydrazide are summarized in Table I. Included also are the values for the corresponding compounds of the D-galactose and D-manno-D-*gala*-heptose[6] series, both of which require a reversal in sign of rotation for comparison with the 7-deoxy-L-manno-L-*gala*-heptose series. The molecular rotations of corresponding compounds in the D-galactose and 7-deoxy-L-manno-L-*gala*-heptose series are fairly near each other with the exception of the α-acetates of the sugars and the methyl glycopyranoside acetates where they are considerably higher in the 7-deoxy-L-manno-L-*gala*-heptose series. The rotations in the 7-deoxy-L-manno-L-*gala*-heptose series are in good or fair agreement with rotations in the D-manno-D-*gala*-heptose series.



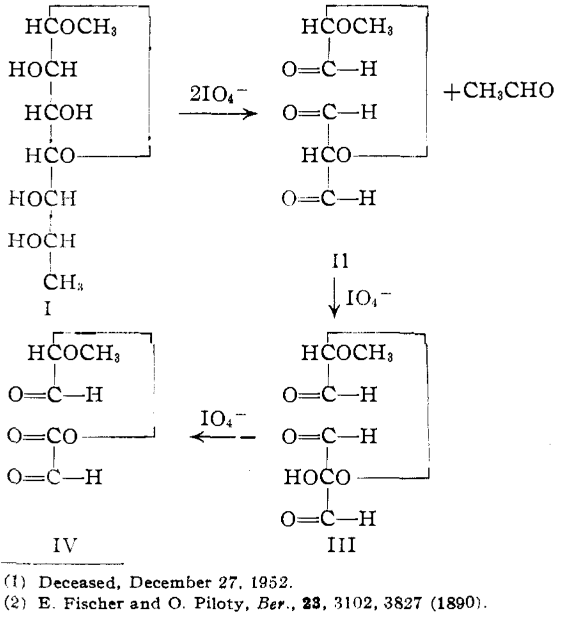
$$\mathrm{HOH_2C{-}\overset{OH}{\underset{H}{C}}{-}\overset{H}{\underset{OH}{C}}{-}\overset{H}{\underset{OH}{C}}{-}\overset{OH}{\underset{H}{C}}{-}CHO}$$

L-Galactose



$$\mathrm{CH_3{-}\overset{OH}{\underset{H}{C}}{-}\overset{OH}{\underset{H}{C}}{-}\overset{H}{\underset{OH}{C}}{-}\overset{H}{\underset{OH}{C}}{-}\overset{OH}{\underset{H}{C}}{-}CHO}$$

7-Deoxy-L-manno-L-*gala*-heptose



Acknowledgment.—We are indebted to Mr. W. D. Chase, Dr. R. T. K. Cornwell and Dr. F. H. Goldman for the analyses.

Experimental[7]

7-Deoxy-L-manno-α-L-*gala*-heptose.—The sugar was prepared in 60–65% yield by reduction of 7-deoxy-L-manno-L-*gala*-heptonic lactone[4] with 2.5% sodium amalgam. The sample used for mutarotation crystallized from water as small prisms during concentration of its solution by spontaneous evaporation at room temperature; it was dried in an evacuated desiccator over calcium chloride; m.p. 186.5–

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(1) Deceased, December 27, 1952.

(2) E. Fischer and O. Piloty, *Ber.*, **23**, 3102, 3827 (1890).

(3) R. C. Hockett, M. H. Nickerson and W. R. Reeder, THIS JOURNAL, **66**, 472 (1944); C. F. Huebner, R. Lohmar, R. J. Dimler, S. Moore and K. P. Link, *J. Biol. Chem.*, **159**, 503 (1945); C. Niemann and J. T. Hays, THIS JOURNAL, **67**, 1302 (1945); C. F. Huebner, S. R. Ames and E. C. Bubl, *ibid.*, **68**, 1621 (1946).

(4) E. L. Jackson and C. S. Hudson, THIS JOURNAL, **56**, 2455 (1934).

(5) The present paper is a sequel to our article on certain derivatives of L-α-rhamnohexonic acid, ref. 4. With the exception of the periodate oxidations the work was completed in 1931.

(6) E. M. Montgomery and C. S. Hudson, THIS JOURNAL, **64**, 247 (1942).

(7) Melting points are corrected.

TABLE I

COMPARISON OF ROTATIONS OF SUBSTANCES IN THE D-GALACTOSE, 7-DEOXY-L-MANNO-L-*gala*-HEPTOSE AND D-MANNO-D-*gala*-HEPTOSE SERIES

Solvent: chloroform (C) or water (W)

	D-Galactose series[a]		7-Deoxy-L-manno-L-*gala*-heptose series		D-Manno-D-*gala*-heptose series[b]	
	$[\alpha]^{20}D$	$[M]^{20}D$	$[\alpha]^{20}D$	$[M]^{20}D$	$[\alpha]^{20}D$	$[M]^{20}D$
Sugar (W) initial	+150.7	+27,200	−128.6	−24,950	+124.0	+26,000
Sugar (W) final	+80.2	+14,500	−62.5	−12,130	+68.9	+14,500
Aldonic acid amide (W)	+30.2	+5,900	−19.9	−4,160	+28.0	+6,300
Aldonic acid phenylhydrazide (W)	+11.0	+3,100	−5.2	−1,560	+21	+6,600
Aldonic acid lactone (W)	−77.6	−13,800	+87.3	+16,780	−74.2	−15,400
Sugar acetate (C) α-	+106.7	+41,700	−135.6	−54,780	+120.8	+55,800
Sugar acetate (C) β-	+25	+9,800	−30.7	−12,400	+34	+15,700
Acetobromo, α- (C)	+236[c]	+97,000[c]	−249.0	−105,820	+208	+100,500
Acetochloro, α- (C)	+212	+77,800	−208.3	−79,360	+175	+76,800
Methyl glycopyranoside (W) α-	+196.1	+38,100	−173.9	−36,170	+178	+39,900
Methyl glycopyranoside (W) β-	+0.7	+100	+18.5	+3,850	−5.1	−1,100
Methyl glycofuranoside, β- (W)	−97.2[d]	−20,200[d]	+117.3	+24,400	−111	−24,600
Methyl glycopyranoside acetate (C) α-	+133.0	+48,200	−157.7	−59,300	+149.5	+65,000
Methyl glycopyranoside acetate (C) β-	−14.0	−5,100	−13.8	−5,190	+8.3	+3,600
Methyl glycofuranoside acetate, β- (C)	−50.5[d]	−19,000[d]	+45.6	+17,150	−43.5	−18,900

[a] References to rotations in the D-galactose series are cited by Montgomery and Hudson, ref. 6, Table II. [b] E. M. Montgomery and C. S. Hudson, ref. 6, Table II. [c] In benzene. [d] Methyl D-galactofuranoside and its acetate are not crystalline; the specific and molecular rotations are for ethyl D-galactofuranoside and its acetate [H. H. Schlubach and K. Meisenheimer, *Ber.*, **67**, 429 (1934)].

187.5°. The sugar mutarotated in water (c 2.48) at 20–21° to $[\alpha]D$ −62.5°, the velocity ($k \times 10^3$) being 6.56 → 5.64 (average = 6.1) calculated as unimolecular in minutes and decimal logarithms.

Anal. Calcd. for $C_7H_{14}O_6$: C, 43.27; H, 7.27. Found: C, 43.09; H, 7.24.

7-Deoxy-L-manno-α-L-*gala*-heptose Pentaacetate.—A mixture of 5 g. of powdered 7-deoxy-L-manno-α-L-*gala*-heptose, 25 cc. of pyridine and 25 cc. of acetic anhydride was shaken for 2 hours at 0° and then kept for 10 days at 5–10° with occasional shaking. The solution was decanted from 0.6 g. of sugar and poured into 500 cc. of ice-water. After partial neutralization with sodium bicarbonate, 7.5 g. of pentaacetate with $[\alpha]^{18}D$ −116.5° in chloroform was collected. The yield was increased to 89% by isolating the product from the filtrate in the usual way with chloroform as solvent. Recrystallized to constant rotation from 80% ethanol and dried *in vacuo* over calcium chloride, the well-built, short prisms showed m.p. 93.5–94.5° and $[\alpha]^{20}D$ −135.6° in chloroform (c 2.1).

Anal. Calcd. for $C_{17}H_{24}O_{11}$: C, 50.47; H, 5.98; CH_3CO, 53.22. Found: C, 50.54; H, 5.99; CH_3CO, 53.51.

7-Deoxy-L-manno-β-L-*gala*-heptose Pentaacetate.—A mixture of 30 g. of powdered 7-deoxy-L-manno-α-L-*gala*-heptose, 7.5 g. of fused sodium acetate and 120 cc. of acetic anhydride was kept at 73–75°, with shaking, until most of the sugar had dissolved and thereafter on the steam-bath for one hour. The products, isolated by the customary procedure, consisted of 48.2 g. or 77% of somewhat impure β-pentaacetate with $[\alpha]^{20}D$ −39.6° in chloroform and 13 g. of sirup from which 0.9 g. of almost pure α-pentaacetate was separated with the use of 50% ethanol. The β-pentaacetate crystallized from 70–90% ethanol as plates which, after being dried at 76° *in vacuo*, melted at 108–108.5° and showed $[\alpha]^{20}D$ −30.7° in chloroform (c 3.6). Recrystallization from ether produced no change in these values.

Anal. Calcd. for $C_{17}H_{24}O_{11}$: C, 50.47; H, 5.98; CH_3CO, 53.22. Found: C, 50.40; H, 5.99; CH_3CO, 52.95.

The β-pentaacetate is transformed to the α-pentaacetate by a mixture of acetic anhydride, acetic acid and sulfuric acid. The rotation of 24 cc. of solution of 4 g. of β-pentaacetate in the isomerizing reagent[8] became constant at $[\alpha]^{23}D$ −131° during 5 hours at 23°. The isolated α-pentaacetate (2.9 g. with $[\alpha]^{20}D$ −125.4° in chloroform), after one recrystallization from 80% ethanol, showed $[\alpha]^{20}D$ −135.7° in chloroform (c 1.0) and melted at 93.5–94.5° alone or mixed with authentic α-pentaacetate.

Tetraacetyl-7-deoxy-L-manno-α-L-*gala*-heptosyl Bromide.—Treatment of 48 g. of dry β-pentaacetate with a solution of hydrogen bromide in glacial acetic acid by the usual procedure produced an 80% yield of tetraacetyl-7-deoxy-L-manno-α-L-*gala*-heptosyl bromide. Recrystallized as stout prisms from ether–petroleum ether (b.p. 30–75°) at 0° and dried *in vacuo* over calcium chloride, the pure compound melted at 113–113.5° and showed $[\alpha]^{20}D$ −249.0° in chloroform (c 2.2).

Anal. Calcd. for $C_{15}H_{21}BrO_9$: Br, 18.80. Found: Br, 18.96.

Tetraacetyl-7-deoxy-L-manno-α-L-*gala*-heptosyl Chloride.—A solution of 2.7 g. of tetraacetyl-7-deoxy-L-manno-α-L-*gala*-heptosyl bromide and 1.7 g. of mercuric chloride in 51 cc. of benzene was refluxed for 2 hours according to Brigl,[9] then kept at 5–10° for one hour, and the mercuric bromide filtered off. The filtrate was extracted with saturated sodium chloride solution, washed with water, dried over calcium chloride and evaporated *in vacuo* to dryness. Recrystallization of the crude product from ether–petroleum ether (1:1) at 0° gave a 92% yield of almost pure compound. After completion of purification from the same solvents and drying *in vacuo* over calcium chloride, the stout prisms melted at 106–107° and showed $[\alpha]^{20}D$ −208.3° in chloroform (c 1.8).

Anal. Calcd. for $C_{15}H_{21}ClO_9$: Cl, 9.31. Found: Cl, 9.25.

Formation of Three Methyl 7-Deoxy-L-manno-L-*gala*-heptosides.—A solution of 200 g. of pure 7-deoxy-L-manno-L-*gala*-heptose in 6000 cc. of absolute methanol containing 1.2% hydrogen chloride was refluxed for 9 hours, the rotation having become constant. After neutralization with *ca.* 300 g. of silver carbonate, addition of carbon and filtration, the solution was concentrated *in vacuo* to 400 cc., then mixed with 400 cc. of acetone and kept at 5–10° for 4 hours when most of the methyl 7-deoxy-L-manno-β-L-*gala*-heptofuranoside had crystallized. The crystals were collected and the filtrate was concentrated *in vacuo* to a thick sirup, most of which crystallized when shaken with 600 cc. of hot acetone added in small portions. The filtrate from these crystals gave more crystals to make the yield of mixed glycosides 87%, which was divided into the following fractions that will be referred to under the individual glycosides: 19 g. with $[\alpha]^{20}D$ +101° in water, 92 g. (−149°), 55 g. (−42°) and 21 g. (−79°). Acetylation of the residual sirup with cold acetic anhydride and pyridine yielded 5 g. of crystalline methyl 7-deoxy-L-manno-α-L-*gala*-heptopyranoside tetraacetate and 9 g. of methyl 7-deoxy-L-manno-β-L-*gala*-heptopyranoside tetraacetate.

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(8) E. M. Montgomery and C. S. Hudson, THIS JOURNAL, **56**, 2463 (1934).

(9) P. Brigl, *Z. physiol. Chem.*, **116**, 50 (1921).

Methyl 7-Deoxy-L-manno-α-L-*gala*-heptopyranoside.—Recrystallization from methanol of the 92 g. of mixed glycosides rotating −149° afforded 73 g. with $[\alpha]^{20}D$ −165° to −170° in water. After purification to constant rotation and drying at 76° *in vacuo* over phosphorus pentoxide, the platelets melted at 131.5–132° and showed $[\alpha]^{20}D$ −173.9° in water (*c* 3). These values were unchanged by recrystallization from 2-propanol, ethyl acetate, butanone and mixtures of methanol with ethyl acetate, butanone or acetone. The glycoside prepared from pure methyl 7-deoxy-L-manno-α-L-*gala*-heptopyranoside tetraacetate showed agreeing figures. Nine grams of tetraacetate was deacetylated with barium methoxide to yield 4 g. or 80% of the glycoside with $[\alpha]^{20}D$ −172.5°. After completion of purification it melted at 131.5–132° and showed $[\alpha]^{20}D$ −173.7° in water. The hydrolysis of the glycoside by 0.05 *N* hydrochloric acid (*c* 1.9) at 99–100° was unimolecular (*k* = 0.00153 determined polarimetrically and calculated in minutes and common logarithms). The glycoside is soluble in cold methanol and 2-propanol; it is difficultly soluble in hot acetone, ethyl acetate and butanone.

Anal. Calcd. for $C_8H_{16}O_6$: C, 46.13; H, 7.75; OCH_3, 14.91. Found: C, 46.16; H, 7.88; OCH_3, 14.69.

Methyl 7-Deoxy-L-manno-β-L-*gala*-heptopyranoside.—Eight grams of crystals with $[\alpha]^{20}D$ +11° to +15° in water was separated from the 55 g. of mixed glycosides rotating −42° by fractional recrystallization from methanol and acetone–methanol. After completion of purification from acetone–methanol and drying at 76° *in vacuo* over phosphorus pentoxide, the long prismatic needles melted at 143.5–144° and showed $[\alpha]^{20}D$ +18.8° in water (*c* 1.5). Because of the small yield of β-isomer by this procedure, it is advantageous to prepare it by way of tetraacetyl-7-deoxy-L-manno-α-L-*gala*-heptosyl bromide. Deacetylation of 10 g. of pure methyl 7-deoxy-L-manno-β-L-*gala*-heptopyranoside tetraacetate, prepared as described below from the tetraacetylheptosyl bromide, with barium methoxide and recrystallization of the product from acetone–methanol afforded an 85% yield of pure β-isomer, which melted at 143.5–144° and showed $[\alpha]^{20}D$ +18.5° in water. The glycoside is readily soluble in cold methanol and difficultly soluble in hot acetone. Its hydrolysis by 0.05 *N* hydrochloric acid (*c* 1.8) at 99–100° was unimolecular (*k* = 0.00172 determined polarimetrically).

Anal. Calcd. for $C_8H_{16}O_6$: C, 46.13; H, 7.75; OCH_3, 14.91. Found: C, 46.17; H, 7.74; OCH_3, 14.57.

Methyl 7-Deoxy-L-manno-β-L-*gala*-heptofuranoside.—The 19 g. of mixed glycosides rotating +101° yielded by recrystallization from methanol to constant rotation prismatic needles of the pure furanoside which, after being dried at 70° *in vacuo*, melted at 179–180° and showed $[\alpha]^{20}D$ +117.3° in water (*c* 3.2). Refluxing gently for 30 minutes a solution of 20 g. of 7-deoxy-L-manno-L-*gala*-heptose in 1260 cc. of methanol containing 1.2% hydrogen chloride afforded a non-reducing solution from which was isolated a 48% yield of almost pure furanoside and 15% of methyl 7-deoxy-L-manno-α-L-*gala*-heptopyranoside. The furanoside is soluble in cold methanol and difficultly soluble in hot acetone. Its hydrolysis by 0.05 *N* hydrochloric acid (*c* 2.1) at 99–100° was unimolecular (*k* = 0.0245 determined polarimetrically).

Anal. Calcd. for $C_8H_{16}O_6$: C, 46.13; H, 7.75; OCH_3, 14.91. Found: C, 46.14; H, 7.82; OCH_3, 14.47.

Sodium Metaperiodate Oxidation of Methyl 7-Deoxy-L-manno-α-L-*gala*-heptopyranoside, Methyl 7-Deoxy-L-manno-β-L-*gala*-heptopyranoside and Methyl 7-Deoxy-L-manno-β-L-*gala*-heptofuranoside.—Prior to oxidation, samples of the pure glycosides were dried at 79° *in vacuo*. Aqueous solutions of 0.09 g. of the methyl α- and of the methyl β-pyranoside were mixed with 7 cc. of 0.198 *M* sodium metaperiodate solution and then diluted with water to 25 cc. After 19 hours at 26° the methyl α-pyranoside showed the consumption on a molar basis of 2.00 moles of the oxidant and the methyl β-pyranoside 1.99 moles. An aqueous solution of 0.0982 g. of the furanoside was mixed with 15 cc. of 0.198 *M* sodium metaperiodate solution and diluted with water to 25 cc. After 23 hours at 26° the consumption of the oxidant on a molar basis was 5.7 moles and after 43 hours 5.94 moles.

Methyl 7-Deoxy-L-manno-α-L-*gala*-heptopyranoside Tetraacetate.—The acetylation of 10 g. of pure methyl 7-deoxy-L-manno-α-L-*gala*-heptopyranoside with a mixture of 40 cc. of acetic anhydride and 40 cc. of pyridine at 0–5° during 17 hours and then pouring the mixture into 500 cc. of ice-water gave 16.2 g. or 90% of crystalline tetraacetate with $[\alpha]^{20}D$ −155.7° in chloroform. An additional 1 g. of product was isolated from the filtrate. The tetraacetate, after being recrystallized to constant rotation from 90% ethanol and dried at 76° *in vacuo* over phosphorus pentoxide, melted at 123.5–124° and showed $[\alpha]^{20}D$ −157.7° in chloroform (*c* 2.2). These values were unchanged by several recrystallizations from ether and from 80% methanol. The compound crystallizes from ethanol as slender prisms and from ether as six-sided prisms.

Anal. Calcd. for $C_{16}H_{24}O_{10}$: C, 51.04; H, 6.43; OCH_3, 8.25; CH_3CO, 45.74. Found: C, 51.03; H, 6.49; OCH_3, 8.06; CH_3CO, 45.67.

Methyl 7-Deoxy-L-manno-β-L-*gala*-heptopyranoside Tetraacetate.—A solution of 35.5 g. of tetraacetyl-7-deoxy-L-manno-α-L-*gala*-heptosyl bromide in 350 cc. of methanol, shaken for 5 minutes with 36 g. of dry silver carbonate and the mixture refluxed for 1 hour, afforded almost the theoretical amount of the tetraacetate which was crystallized from ether. After recrystallization as slender prisms from ethanol and drying at 76° *in vacuo* over phosphorus pentoxide, the tetraacetate melted at 157–157.5° and showed $[\alpha]^{20}D$ −13.8° in chloroform (*c* 3.2). Further recrystallization from ethanol and from ether caused no change in these values.

Anal. Calcd. for $C_{16}H_{24}O_{10}$: C, 51.04; H, 6.43; OCH_3, 8.25; CH_3CO, 45.74. Found: C, 51.10; H, 6.45; OCH_3, 8.01; CH_3CO, 45.54.

Methyl 7-deoxy-L-manno-β-L-*gala*-heptopyranoside tetraacetate was transformed to methyl 7-deoxy-L-manno-α-L-*gala*-heptopyranoside tetraacetate by reaction with titanium tetrachloride. A solution of 5.4 g. of titanium tetrachloride and 10.7 g. of the β-tetraacetate in 140 cc. of absolute chloroform yielded by Pacsu's directions,[10] refluxing for 11.5 hours, a sirup from which was isolated with the use of ether–petroleum ether a 50% yield of crystals in fractions with $[\alpha]^{20}D$ −146° to −157° in chloroform. Several recrystallizations from ether and from 95% ethanol gave the pure α-tetraacetate which showed $[\alpha]^{20}D$ −157.5° in chloroform and melted at 123.5–124°.

Methyl 7-Deoxy-L-manno-β-L-*gala*-heptofuranoside Tetraacetate.—Eight grams of pure methyl 7-deoxy-L-manno-β-L-*gala*-heptofuranoside was dissolved in a mixture of 32 cc. of acetic anhydride and 32 cc. of pyridine by shaking for 1 hour at 25° and this solution was kept at 0–5° for 17 hours. The product was crystallized from ether–petroleum ether; yield 13.6 g. or 94% with $[\alpha]^{20}D$ +46.0° in chloroform. After further recrystallization from ether–petroleum ether and from 90% ethanol, the dried well-formed prisms melted at 83° and showed $[\alpha]^{20}D$ +45.6° in chloroform (*c* 4.2).

Anal. Calcd. for $C_{16}H_{24}O_{10}$: C, 51.04; H, 6.43; OCH_3, 8.25; CH_3CO, 45.74. Found: C, 51.15; H, 6.34; OCH_3, 8.19; CH_3CO, 45.66.

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[10] E. Pacsu, *Ber.*, **61**, 1508 (1928); THIS JOURNAL, **52**, 2563 (1930).