The spectrum of *meso*-cystine is clearly that of two species, present in comparable amounts, but with slightly different n.m.r. parameters. The analysis of this spectrum is given in Table I where the two species present are labeled a and b. Unfortunately, under these conditions the spectral lines are rather broad, and resolution is affected. This poor resolution is reflected in the uncertainty of the derived constants. It must be assumed that one species in this spectrum is L-cystine, and the other *meso*-cystine. However, the precision of the values for the constants does not appear to allow an assignment of a or b to *meso*-cystine. The conclusion must still be drawn that even at this pH, *meso*- and L-cystine have different structures. The peak assigned to cysteine in the previous paragraph is also present in this spectrum. The spectra of the methyl esters was not obtained at this pH due to very rapid hydrolysis.

Discussion

In view of the original question these observations indicate that the stabilization of the actual configuration of L-cystine in acid solution is due to intramolecular interaction between the two moieties. This binding appears to be absent in *meso*-cystine as evidenced by the equivalence of the spectrum of *meso*-cystine with that of the esters of both L- and *meso*-cystine. Additional evidence is the very large decrease in δ_{ab} from L-cystine to *meso*-cystine in acid solution, indicating that the β protons have become almost equivalent magnetically in *meso*-cystine. This suggests that the moieties in *meso*-cystine rotate about the disulfide bond much more freely than in L-cystine. This is in accord with the difference in the number of possible stabilizing bonds as discussed in the introduction.

It is interesting that the coupling constants J_{ax} and J_{bx} are relatively invariant to changes in pH for L- and *meso*-cystine and are comparable to those of L-cysteine even though structural changes have clearly taken place. It appears probable, therefore, that the classical rotamer analysis does not apply to the cystines. It should be mentioned here that the spectra of *meso*-cystine and the two methyl esters will equally well fit a six-line A_2B analysis in which the derived constants are $\delta_{aa} \equiv 0$ c.p.s. and $N = 5.9$ c.p.s. Only the presence of the very weak satellites indicate that the system should be more properly regarded as an ABX system with $\delta_{ab} << J_{ab}$.

No conclusion can be drawn as to the stability of either structure I or II so far as the configuration about the disulfide bond is concerned. If the exact nature of the optical rotatory activity of the disulfide transition becomes known it should be possible to combine this knowledge with further n.m.r. measurements to indicate which configuration, left- or right-hand helix, has the lowest energy.

A New Method for the Synthesis of Furanose Derivatives of Aldohexoses[1]

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Contribution from the Department of Biological Chemistry, University of Illinois at the Medical Center, Chicago, Illinois. *Received July 12, 1965*

Disiamylborane was used to reduce tetraacylhexono-γ-lactones to the corresponding tetraacylhexofuranoses. Reduction is almost quantitative and the blocking ester groups are unaffected. The reaction was applied to the newly prepared tetra-O-benzoyl-γ-lactones of L-*gulose,* D-*gulose,* D-*allose,* D-*talose, and* D-*altrose and to* D-*galactono-γ-lactone tetraacetate resulting in the corresponding acylated tetraacylhexofuranoses which were acylated at the anomeric hydroxyl group to form pentaacylhexofuranoses. This method was developed as a general procedure of short reaction route to obtain furanose derivatives of aldoses. It has a potentially important application in biochemistry which lies in its use for the preparation of C-1′ labeled furanosyl nucleosides.*

Hexoses exist primarily in the pyranose ring form, and no general method for obtaining furanose derivatives of hexoses has heretofore been reported. For this purpose special methods have been employed utilizing isopropylidene derivatives to prepare 9-β-D-glucofuranosyladenine[2] and other furanosyl nucleosides of 6-deoxy hexoses.[3] Recently Wolfrom, *et al.*,[4] reported on the use of furanose thioglycosides for the preparation of hexofuranosyl nucleosides of D-glucose and D-galactose. Although these methods may be more generally applicable in many instances, as with the rare hexoses, such intermediates are as yet unknown or the pathway might not be desirable as a practical reaction sequence.

For these reasons, and in view of the advantages of having a single method applicable to a wide variety of carbohydrates, and because of our interest in the prep-

(1) (a) Taken in part from a thesis submitted by L. M. Lerner to the University of Illinois Graduate College in partial fulfillment of the requirements for the Ph.D. degree. (b) Supported in part by Grant P-161 from the American Cancer Society and by Training Grant No. GM-471 from the Division of General Medical Sciences of the U. S. Public Health Service.

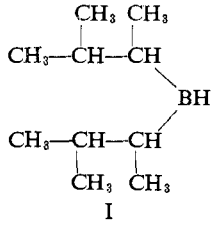
(2) E. J. Reist, R. R. Spencer, and B. R. Baker, *J. Org. Chem.*, **23**, 1958 (1958).

(3) E. J. Reist, R. R. Spencer, and B. R. Baker, *ibid.*, **23**, 1753 (1958); E. J. Reist, R. R. Spencer, and B. R. Baker, *ibid.*, **23**, 1757 (1958); B. R. Baker and K. Hewson, *ibid.*, **22**, 966 (1957); E. J. Reist, L. Goodman, R. R. Spencer, and B. R. Baker, *J. Am. Chem. Soc.*, **80**, 3962 (1958); E. J. Reist, L. Goodman, and B. R. Baker, *ibid.*, **80**, 5775 (1958); P. A. Levene and I. E. Muskat, *J. Biol. Chem.*, **106**, 761 (1934).

(4) M. L. Wolfrom, P. McWain, R. Pagnucco, and A. Thompson, *J. Org. Chem.*, **29**, 454 (1964); M. L. Wolfrom and P. McWain, *ibid.*, **30**, 1099 (1965).

aration of hexofuranosyl nucleosides, it appeared desirable to take advantage of the furan ring already existent in γ-aldonolactones as a means of obtaining furanose derivatives. This appeared to be a particularly fruitful line of attack since the γ-lactones of the hexonic acids and other aldonic acids are readily obtainable. The procedure that has been used consists of esterifying the free hydroxyl groups of the γ-lactones and reducing the lactone to a hemiacetal. The critical step entailed the use of an agent which would reduce the lactone, an inner ester, without reducing the ester blocking groups which would permit rearrangement to the more stable pyranose ring. Initial attempts to reduce aqueous suspensions of tetra-O-acetyl-D-galactono-γ-lactone and tetra-O-benzoyl-D-gulono-γ-lactone by classical methods using sodium amalgam or sodium borohydride yielded only traces of furanose, although solutions of free lactones usually can be reduced to pyranoses in 70–90% yield. Solutions of the lactone in aqueous organic solvents failed to result in more than 5% yields of the products. Yields of reducing sugar were determined by a modified anthrone test[5] which was carried out after removal of the blocking ester groups by methanolic sodium methoxide in chloroform solution and extraction of the sugar into water. The results were found to be dependable, applicable to all carbohydrates tested, and showed no interference by lactones.

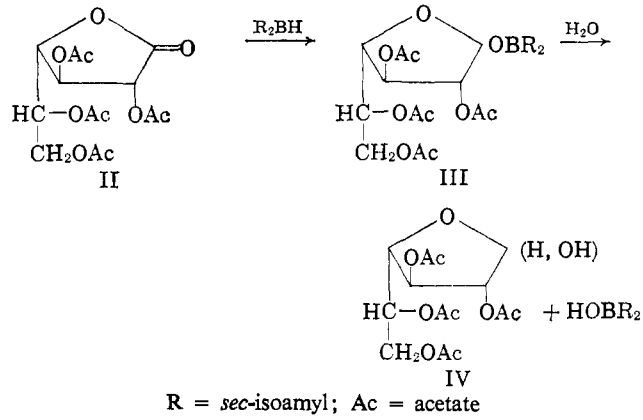
In 1961, Brown and Bigley[6] reported that γ-lactones could be reduced to hydroxyaldehydes with bis-3-methyl-2-butylborane (di-*sec*-isoamylborane; disiamylborane) (I) and indicated that γ-butyrolactone and



I

γ-valerolactone had been reduced to the corresponding hydroxyaldehydes in about 70% yield. It was also reported that esters were not affected by the reagent. It appeared, therefore, that this reagent might be effective in bringing about the desired reduction of acylated sugar lactones. Zweifel, *et al.*,[7] reported that they prepared the reagent at 0°, but we experienced considerable difficulty at that temperature. At a temperature of −10°, however, disiamylborane was formed in good yield in 6 hr. by mixing stoichiometric amounts of borane and 2-methyl-2-butene in tetrahydrofuran solution.

Initially the reduction was applied to D-galactono-γ-lactone tetraacetate and D-gulono-γ-lactone tetrabenzoate.[8] The reaction sequence, which has been discussed by Brown,[9] is shown here for D-galactono-γ-lactone tetraacetate (II). In the process, disiamylborane



II III IV

R = *sec*-isoamyl; Ac = acetate

is added across the carbonyl group to donate its hydrogen to the anomeric carbon atom and, simultaneously, an oxygen–boron bond is formed. This bond is easily hydrolyzed to form the hemiacetal (IV). Oxidation with H_2O_2 at pH 7–8 converts the dialkylborinic acid by-product to boric acid and 3-methyl-2-butanol,[10] which are easily separated from the product during the work-up.

Hydroboration reactions proceed slowly in most organic solvents, but they are catalyzed by ethers.[9] The exact mechanism of the reaction is unknown, but kinetic data have revealed a direct role of the ether. Disiamylborane in tetrahydrofuran exists as the dimer, and the solvent apparently acts by aiding in the removal of a disiamylborane monomer from the reaction site.[9] The reduction can therefore be carried out in ethyl ether, tetrahydrofuran, diethylene glycol dimethyl ether (diglyme), or triethylene glycol dimethyl ether (triglyme). In the work reported here tetrahydrofuran was the ether solvent of choice because it readily dissolves diborane and most of the tetraacyl lactones. It is also low boiling and easily evaporated and is quite miscible with water, allowing the subsequent hydrolysis and work-up to proceed easily and mostly in one phase.

All of the aldono-γ-lactone tetrabenzoates reported here are new compounds and were prepared by the method of Levene and Meyer,[11] with modifications when necessary. Physical constants of these compounds are summarized in Table I.

Table I. Optical Rotation and Melting Points of Hexono-γ-lactone Tetrabenzoates

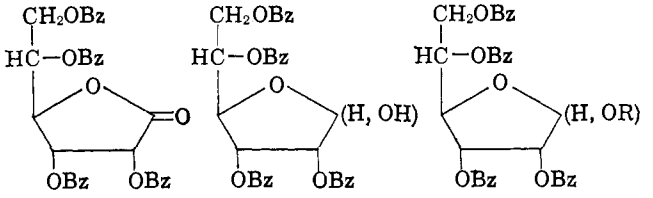
Carbohydrate	$[\alpha]_D$, deg.	M.p., °C.
L-Gulono-	+87.8	157–157.5
D-Gulono-	−89.3	155–156
D-Allono-	−20.0	114–115
D-Talono-	−3.38	134–135
D-Altrono-	−69.8	189–190

Tetrahydrofuran solutions (usually 0.25 *M*) of the hexono-γ-lactone tetrabenzoates (V) were reduced in the presence of a fourfold excess of disiamylborane at room temperature for 14–20 hr. under an atmosphere of dry nitrogen. D-Altrono-γ-lactone tetrabenzoate, however, is only slightly soluble in tetrahydrofuran and

(5) L. C. Mokrasch, *J. Biol. Chem.*, 208, 55 (1954); W. E. Trevelyan and J. S. Harrison, *Biochem. J.*, 50, 298 (1952).
(6) H. C. Brown and D. B. Bigley, *J. Am. Chem. Soc.*, 83, 486 (1961).
(7) G. Zweifel, K. Nagase, and H. C. Brown, *ibid.*, 84, 190 (1962).
(8) P. Kohn, R. H. Samaritano, and L. M. Lerner, *ibid.*, 86, 1457 (1964); Abstracts of Papers, 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964, p. 19D.
(9) H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.
(10) H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, 78, 5694 (1956); J. R. Johnson and M. G. Van Campen, *ibid.*, 60, 121 (1938).
(11) P. A. Levene and G. M. Meyer, *J. Biol. Chem.*, 76, 513 (1928).

other ethers and was therefore dissolved in methylene dichloride. This solution was added dropwise to the tetrahydrofuran solution of disiamylborane, resulting in the formation of a white suspension. Complete dissolution occurred as the reaction proceeded.

When the reaction was completed, water was added to produce the tetraacylaldofuranoses (VI). To the resulting mixture, hydrogen peroxide was added at 0° and pH 7–8, maintained by simultaneous addition of 3 *N* sodium hydroxide.



aldono-γ-lactone tetrabenzoate	aldofuranose tetrabenzoate	pentaacyl-aldofuranose
Va, L-gulono-	VIa, L-gulo-	VIIa, L-gulo-
b, D-gulono-	b, D-gulo-	b, D-gulo-
c, D-allono-	c, D-allo-	c, D-allo-
d, D-talono-	d, D-talo-	d, D-talo-
e, D-altrono-	e, D-altro-	e, D-altro-

Bz = benzoate; R = acetate for VIIa,b, and *p*-nitrobenzoate for VIIc,d,e

The results of the reduction reaction, shown in Table II, indicate that the reaction proceeds in excellent yield.

Table II. Reduction of Tetrabenzoyl-γ-lactones to Tetrabenzoylhexofuranoses

γ-Lactone reduced	Yield, % By anthrone determination	Yield, % As crystalline product
L-Gulono-	100	88
D-Gulono-	100	97
D-Galactono-[a]	83	Syrup
D-Allono-	90	90
D-Talono-	81	Syrup
D-Altono-	92	Syrup

[a] Tetraacetyl ester.

Following reduction, the anomeric hydroxyl group was acylated. Acetic anhydride in pyridine was used to prepare 1-O-acetyl-2,3,5,6-tetra-O-benzoyl-L-gulofuranose (VIIa) and 1-O-acetyl-2,3,5,6-tetra-O-benzoyl-D-gulofuranose (VIIb). β-D-Galactofuranose pentaacetate was also prepared by this route. The 1-O-acetates and 1-O-benzoates of the other aldofuranose derivatives could not be obtained crystalline. *p*-Nitrobenzoyl chloride in pyridine was therefore used to prepare crystalline 1-O-*p*-nitrobenzoyl-2,3,5,6-tetra-O-benzoyl-D-allofuranose (VIIc), 1-O-*p*-nitrobenzoyl-2,3,5,6-tetra-O-benzoyl-D-talofuranose (VIId), and 1-O-*p*-nitrobenzoyl-2,3,5,6-tetra-O-benzoyl-D-altrofuranose (VIIe). In the last two cases only a small portion of the product (20–30%) would crystallize.

The reduction of polyacyl esters of aldono-γ-lactones is potentially useful in biochemical studies of nucleosides since it provides a simple means of introducing isotopes into the anomeric position of the carbohydrate moiety. Carbon-14 can be introduced during preparation of the lactones *via* the Fischer–Kiliani cyanohydrin synthesis by the use of $^{14}CN^-$, or tritium can be introduced by the use of sodium borotritide in the preparation of disiamylborane. The preparation and properties of hexofuranosyladenine nucleosides, synthesized from the hexofuranosyl esters reported here, will be described in a subsequent report.

Experimental Section[12]

Melting points were obtained on a Kofler micro hot stage and correspond to corrected values. Optical rotations were determined in 100-mm. semimicro tubes using a Rudolph Model 70 polarimeter. Infrared spectra were measured on a Perkin-Elmer Infracord spectrophotometer, and optical densities of colored solutions in the visible range were obtained with a Coleman Junior spectrophotometer. Paper chromatograms of aqueous solutions of reducing sugars and their corresponding lactones were run on Whatman No. 2 paper using 1-butanol–acetic acid–water (4:1:5, v./v./v.) organic phase, as the developing solvent. The spots were located with an aniline oxalate spray reagent[13] or with a sodium periodate–potassium permanganate spray reagent.[14] All evaporations of organic solvents were performed *in vacuo* at 40–45° on a rotary evaporator.

Aldono-γ-lactones. D-Allono-γ-lactone was prepared by the method of Pratt and Richtmyer,[15] and the calcium D-altronate obtained by this procedure was used to prepare D-altrono-γ-lactone.[16] D-Talono-γ-lactone was prepared as described by Cretcher and Renfrew.[17] D-Gulono-γ-lactone and D-galactono-γ-lactone were purchased from Pfanstiehl Laboratories. L-Gulono-γ-lactone was prepared from D-glucuronic acid.[18]

Metal Hydrides. Lithium aluminum hydride and sodium borohydride (98+%) were products of Metal Hydrides, Inc. Sodium borohydride of lower purity was purified by the method of Brown, *et al.*[19]

Solvents. Diglyme was obtained from K & K Laboratories, Inc., Plainview, N. Y. Just prior to use it was twice distilled from lithium aluminum hydride at reduced pressure (73°, 35 mm.) under nitrogen. Tetrahydrofuran (Fisher Certified Reagent) was stored over potassium hydroxide pellets. Just before use it was distilled twice (b.p. 65–66°) from lithium aluminum hydride at atmospheric pressure under nitrogen.

Preparation of Diborane.[20] The diborane generator consisted of a distilling flask outfitted with a pressure-equalizing dropping funnel, a magnetic stirring bar, a nitrogen inlet, and an exit for diborane. The diborane and the nitrogen carrier were passed through a trap of

(12) Elemental analyses were determined at the Spang Microanalytical Laboratory, Ann Arbor, Mich., or at Midwest Microlab, Inc., Indianapolis, Ind.

(13) S. M. Partridge, *Biochem. Soc. Symp.*, (Cambridge, Engl.) 3, 52 (1949).

(14) R. U. Lemieux and H. F. Bauer, *Anal. Chem.*, 26, 920 (1954).

(15) J. W. Pratt and N. K. Richtmyer, *J. Am. Chem. Soc.*, 77, 1906 (1955).

(16) C. W. Austin and F. L. Humoller, *ibid.*, 56, 1153 (1934).

(17) L. H. Cretcher and A. G. Renfrew, *ibid.*, 54, 1590 (1932).

(18) F. Erlich and K. Rehorst, *Ber.*, 62, 628 (1929); M. L. Wolfrom and K. Anno, *J. Am. Chem. Soc.*, 74, 5583 (1952).

(19) H. C. Brown, E. J. Mead, and B. C. Subba Rao, 77, 6209 (1955).

(20) H. C. Brown and P. A. Tierney, *ibid.*, 80, 1552 (1958); G. Zweifel, K. Nagase, and H. C. Brown, *ibid.*, 84, 183 (1962).

sodium borohydride in diglyme to remove contaminating boron trifluoride and finally into a receiving flask containing tetrahydrofuran.

In a typical preparation, 114 ml. of 1 *M* sodium borohydride in diglyme was slowly added dropwise and at room temperature to a magnetically stirred solution of 0.228 mole of boron fluoride ethyl ether (Distillation Products), and the generated diborane was collected in 60 ml. of tetrahydrofuran at 0°. After all of the sodium borohydride had been added (about 45 min.), the generator was warmed to 70° to distil residual diborane. The concentration of borane in tetrahydrofuran in different runs was from 1.6 to 2.5 *M*. This was determined by removal of an aliquot, usually 1 ml., which was pipetted into 10 ml. of acetone to form diisopropoxyborane. Addition of 10 ml. of water brought about hydrolysis to boric acid. Mannitol (0.7 g.) was added, and the solution was titrated with standard 0.10 *N* sodium hydroxide solution to a phenolphthalein endpoint.

Preparation of Disiamylborane (Bis-3-methyl-2-butylborane).[20] In a flask equipped with a pressure-equalizing dropping funnel and a nitrogen inlet was placed 25 ml. of 2-methyl-2-butene (0.24 mole, K & K Laboratories), and the flask was immersed in a refrigerated bath at −10°. The borane solution (50 ml., 2.5 *M*) was added dropwise to the magnetically stirred solution. After 6 hr. of stirring under a slight static pressure of nitrogen the solution was diluted to 100 ml. with tetrahydrofuran to give a solution 1.25 *M* in disiamylborane.

Anthrone Determination. An aliquot, usually 1 ml., of a chloroform solution of the tetraacylhexofuranose was treated with 1 ml. of 0.5 *M* methanolic sodium methoxide at 0° for 0.5 hr. Following extraction with water, the water layer was treated batchwise with IR-120 (H^+) ion-exchange resin, filtered through a sintered glass funnel, and diluted to a known volume. Aliquots were removed for the determination of reducing sugars by a modified anthrone method[5] using standards of the sugar in question. The corresponding lactones did not react with this reagent. This procedure, when carried out with D-glucose pentaacetate and D-galactose pentabenzoate, was found to give quantitative yields of the reducing sugars.

Preparation of Tetra-O-acyl-hexono-γ-lactones. The hexono-γ-lactones were benzoylated in the manner described by Levene and Meyer[11] for D-glucose.

L-*Gulono-γ-lactone Tetrabenzoate (Va).* Benzoyl chloride (70 ml.) and 70 ml. of chloroform were mixed and cooled in an ice-salt bath. Similarly, 84 ml. of pyridine and 70 ml. of chloroform were mixed in a separate vessel and cooled in an ice-salt bath, and the two solutions were mixed. The vessel was placed in an ice bath and the solution was stirred with a magnetic stirrer while L-gulono-γ-lactone (20 g., 0.112 mole) was slowly added in small portions. After stirring for 1 hr. at 0° the flask was placed in the refrigerator for 20 hr. After dilution with a large amount of chloroform, the solution was washed three times with saturated sodium bicarbonate solution and three times with distilled water. The chloroform layer was dried over sodium sulfate and concentrated to a syrup. Toluene was added and distilled once, leaving a crystalline mass. The product was crystallized from warm absolute ethanol–chloroform (8:2). A yield of 55.8 g. (84%) was obtained. Recrystallization of a sample gave the analytical material as clusters of glittering needles, m.p. 157–157.5°; $[\alpha]^{22}D$ +87.8° (*c* 4.12, $CHCl_3$); infrared spectrum: λ_{max}^{Nujol} 5.52 (γ-lactone) and 5.8 μ (benzoate carbonyl).

Anal. Calcd. for $C_{34}H_{26}O_{10}$: C, 68.67; H, 4.41. Found: C, 68.81; H, 4.35.

D-*Gulono-γ-lactone Tetrabenzoate (Vb).* This compound was prepared as described for Va. The product was crystallized from warm absolute ethanol. From 20 g. of the γ-lactone 64 g. (96% yield) of product was obtained. An analytical sample, recrystallized from ethanol–chloroform, gave long needles, m.p. 155–156°; $[\alpha]^{21}D$ −89.3° (*c* 4.10, $CHCl_3$); infrared spectrum: λ_{max}^{film} 5.5 (γ-lactone) and 5.8 μ (benzoate carbonyl).

Anal. Calcd. for $C_{34}H_{26}O_{10}$: C, 68.67; H, 4.41. Found: C, 68.62; H, 4.40.

D-*Allono-γ-lactone Tetrabenzoate (Vc).* Benzoylation of the γ-lactone was carried out for 48 hr. as described above. The syrup obtained was dissolved in toluene and the solvent was evaporated to remove traces of pyridine. The product was crystallized from absolute ethanol in 77% yield, m.p. 114–115°; $[\alpha]^{19}D$ −20.0° (*c* 4.00, $CHCl_3$); infrared spectrum: λ_{max}^{film} 5.55 (γ-lactone) and 5.75 μ (benzoate carbonyl).

Anal. Calcd. for $C_{34}H_{26}O_{10}$: C, 68.67; H, 4.41. Found: C, 68.81; H, 4.62.

D-*Talono-γ-lactone Tetrabenzoate (Vd).* D-Talono-γ-lactone was benzoylated as described for Va. Traces of pyridine were removed by evaporation of toluene and the product was crystallized from ethanol after petroleum ether was added to incipient turbidity. Recrystallization from absolute methanol–chloroform deposited large needles. From 1 g. of the γ-lactone 2.36 g. (73% yield) of product was obtained, m.p. 134–135°; $[\alpha]^{19}D$ −3.38° (*c* 3.85, $CHCl_3$); infrared spectrum: λ_{max}^{film} 5.55 (γ-lactone) and 5.80 μ (benzoate carbonyl).

Anal. Calcd. for $C_{34}H_{26}O_{10}$: C, 68.67; H, 4.41. Found: C, 68.81; H, 4.35.

D-*Altrono-γ-lactone Tetrabenzoate (Ve).* Because the starting material was not crystalline the preparation of Ve was modified from the usual procedure.

A syrup (8.1 g.) of altronic acid prepared from calcium altronate[16] was lactonized at 70°, *in vacuo*, for 2 hr. and then dissolved in 75 ml. of pyridine by refluxing with stirring for 10 min. The flask was cooled to 0° and 39 ml. of benzoyl chloride was added very slowly, with stirring. When all of the benzoyl chloride had been added a white precipitate of pyridine hydrochloride formed. Chloroform (75 ml.) was added, and the reaction mixture was stored at room temperature for 20 hr. Ice (2 g.) was added, the mixture was stirred (slight warming), and after 15 min. the contents were transferred to a separatory funnel and washed twice with 150-ml. portions of ice-cold 3 *N* sulfuric acid. The combined washings were back-extracted twice with 50-ml. portions of chloroform which were combined with the main chloroform solution. The chloroform solution was next washed twice with 150-ml. portions of cold, saturated sodium bicarbonate solution which was back-extracted with chloroform. One washing of the combined chloroform solutions with 150 ml. of

water gave an emulsion which was broken by addition of sodium chloride. The volume of chloroform was reduced to 300 ml. by evaporation, and the solution was filtered through a pad of Norit A and Celite 535. The chloroform solution was dried over magnesium sulfate and the solvent was evaporated. The white product precipitated in the concentrated chloroform solution. Absolute ethanol (200 ml.) was added, the contents of the flask were triturated, and the product was removed by filtration. It was crystallized from hot chloroform–ethanol to yield 17.1 g. (63%) of fluffy white needles, m.p. 189–190°, $[\alpha]^{20}D$ −69.8° (*c* 4.04, CH_2Cl_2). This material did not recrystallize well. The crystals became less well defined at each attempt and the melting point dropped. The product was insoluble in methanol and ethanol, rather insoluble in ethyl ether and tetrahydrofuran, moderately soluble in chloroform, and fairly soluble in methylene chloride; infrared spectrum: λ_{max}^{film} 5.55 (γ-lactone) and 5.78 μ (benzoate carbonyl).

Anal. Calcd. for $C_{34}H_{26}O_{10}$: C, 68.67; H, 4.41. Found: C, 68.68; H, 4.41.

*Reduction with Disiamylborane. 2,3,5,6-Tetra-O-benzoyl-*D*-gulofuranose* (*VIb*). To 75 ml. of tetrahydrofuran containing 0.125 mole of disiamylborane in a nitrogen atmosphere was added slowly 17.8 g. (30 mmoles) of Vb in 50 ml. of tetrahydrofuran. After standing under nitrogen overnight at room temperature, 10 ml. of water was slowly added and the mixture was refluxed for 0.5 hr. The solution was cooled to 0° and 20 ml. of 30% hydrogen peroxide was very slowly added dropwise while the pH was maintained between 7 and 8 with 3 *N* sodium hydroxide.[10] The mixture was concentrated to a small volume and extracted several times with chloroform. The chloroform layer was washed with water and dried over calcium chloride. Determination of the reducing sugar content by the anthrone method after de-esterification indicated a 100% yield. Paper chromatography showed only one spot, corresponding to D-gulose. The chloroform was evaporated and the syrup obtained was dissolved in warm absolute ethanol from which the product crystallized to give 17.2 g. (97% yield). A sample was recrystallized to yield the analytical material, m.p. 156–157°; $[\alpha]^{21}D$ −55.3° (*c* 4.03, $CHCl_3$); infrared spectrum: λ_{max}^{film} 2.85 μ (hydroxyl), no lactone peak at 5.5 μ.

Anal. Calcd. for $C_{34}H_{28}O_{10}$: C, 68.40; H, 4.73. Found: C, 67.91; H, 4.60.

*2,3,5,6-Tetra-O-acetyl-*D*-galactofuranose* (*IV*). D-Galactono-γ-lactone tetraacetate (9.0 g., 26 mmoles), prepared by the procedure of Upson, *et al.*,[21] was reduced in the same manner as Vb. The product, which would not crystallize, was obtained in an 83% yield (anthrone); infrared spectrum: λ_{max}^{smear} 2.85 μ (hydroxyl), no lactone peak at 5.6 μ.

*2,3,5,6-Tetra-O-benzoyl-*L*-gulofuranose* (*VIa*). The same procedure was applied to Va. From 50 g. (84 mmoles) of Va 44 g. (88% yield) of white needles was crystallized from warm absolute ethanol. A twice-recrystallized sample had m.p. 153–156°; $[\alpha]^{20}D$ +53.7° (*c* 3.99, $CHCl_3$); infrared spectrum: λ_{max}^{film} 2.85 (hydroxyl) and 5.8 μ (benzoate); no lactone peak at 5.6 μ.

Anal. Calcd. for $C_{34}H_{28}O_{10}$: C, 68.40; H, 4.73. Found: C, 68.44; H, 4.65.

*2,3,5,6-Tetra-O-benzoyl-*D*-allofuranose* (*VIc*). An amount of 43.9 g. (73 mmoles) of Vc was reduced as described above. The resulting syrup was dissolved in a small volume of chloroform, absolute ethanol was added, and then petroleum ether to incipient turbidity. Upon chilling, the product crystallized to give 39.2 g. (90% yield) in two crops, m.p. 144–145°. An analytical sample, recrystallized from ethanol–chloroform, had m.p. 148–149°; $[\alpha]^{20}D$ +83.0° (*c* 4.00, $CHCl_3$); infrared spectrum: λ_{max}^{film} 2.85 μ (hydroxyl), no lactone peak at 5.5 μ.

Anal. Calcd. for $C_{34}H_{28}O_{10}$: C, 68.40; H, 4.73. Found: C, 68.27; H, 4.76.

*2,3,5,6-Tetra-O-benzoyl-*D*-talofuranose* (*VId*). The reduction of Vd (30.5 g.) was carried out in the same manner except that the lower solubility of Vd in tetrahydrofuran made necessary an increase in the volume of solvent used. However, the ratio of reducing reagent to substrate was maintained at 4:1. The product could not be induced to crystallize. The anthrone assay showed the yield to be 81%, and D-talose was recognized as a single spot on a paper chromatogram; infrared spectrum: λ_{max}^{smear} 2.85 μ (hydroxyl), no γ-lactone peak at 5.55 μ.

*2,3,5,6-Tetra-O-benzoyl-*D*-altrofuranose* (*VIe*). Because Ve was insoluble in tetrahydrofuran, 11.3 g. (19 mmoles) of this material was suspended in 100 ml. of methylene chloride, which dissolved most of it. The suspension was added dropwise to a solution of 77 mmoles of disiamylborane in 65 ml. of tetrahydrofuran 0°, under nitrogen. In the course of a few hours at room temperature the suspended material dissolved, and the reaction mixture was allowed to stand for an additional 24 hr. Following hydrolysis and oxidation the organic solvents were evaporated, the product was extracted with methylene chloride, and the layers were clarified by centrifugation. The methylene chloride layer was dried over magnesium sulfate. The yield of product according to the anthrone test was 92%, and a spot corresponding to D-altrose was located on a paper chromatogram. A milky suspension present in the syrup was removed by alumina chromatography which resulted in a clear, colorless syrup that would not crystallize; infrared spectrum: 2.85 μ (hydroxyl), no lactone peak at 5.55 μ.

*Preparation of Pentaacylhexofuranoses. 1-O-Acetyl-2,3,5,6-tetra-O-benzoyl-*L*-gulofuranose* (*VIIa*). An amount of 25 g. (42.1 mmoles) of VIa was dissolved in 250 ml. of pyridine and cooled in an ice bath, and 35 ml. of acetic anhydride was added dropwise with stirring. After 21 hr. at room temperature the reaction mixture was poured into 500 ml. of ice chips and the mixture was stirred. When nearly all of the ice had melted, the product crystallized. Recrystallization from warm absolute ethanol yielded 26.6 g. (98%) of the product, m.p. 131.5–132.5°, $[\alpha]^{22}D$ +56.6° (*c* 3.85, $CHCl_3$).

Anal. Calcd. for $C_{36}H_{30}O_{11}$: C, 67.70; H, 4.74. Found: C, 67.67; H, 4.80.

*1-O-Acetyl-2,3,5,6-tetra-O-benzoyl-*D*-gulofuranose* (*VIIb*). In 50 ml. of pyridine was dissolved 5 g. (8.4

(21) F. W. Upson, J. M. Brackenbury, and C. Linn, *J. Am. Chem. Soc.*, **58**, 2549 (1936).

mmoles) of VIb, the solution was cooled to 0°, and 5 ml. of acetic anhydride was added. After 20 hr. at room temperature several pieces of ice were added to the orange solution. After 15 min. with occasional stirring the solution was concentrated to a syrup which was dissolved in 20 ml. of chloroform. The chloroform solution was washed twice with saturated sodium bicarbonate solution, discharging the orange color into the aqueous phase, and then washed twice with water. The solution was dried over magnesium sulfate and the solvent was evaporated. A hard syrup remained which was dissolved in hot absolute ethanol from which 4.52 g. (85% yield) of product was obtained, m.p. 128–129°. Recrystallization from ethanol yielded the analytical material as feathery white needles, m.p. 131–132°, $[\alpha]^{19}D$ −56.8° (*c* 3.73, $CHCl_3$).

Anal. Calcd. for $C_{36}H_{30}O_{11}$: C, 67.70; H, 4.74. Found: C, 67.93; H, 4.97.

β-D-Galactofuranose Pentaacetate. A syrup (8.8 g.) containing primarily IV was acetylated to give a syrup which crystallized after standing in the refrigerator for 3 weeks. The crystalline and syrupy mass was triturated with cold absolute ethanol and filtered. A 60% yield of β-D-galactofuranose pentaacetate was obtained, m.p. 99–100°, $[\alpha]^{21}D$ −40.5° (*c* 4.00, $CHCl_3$) (lit.[22] m.p. 98°, $[\alpha]^{20}D$ −41.6°).

1-O-p-Nitrobenzoyl-2,3,5,6-tetra-O-benzoyl-D-allofuranose (VIIc). In 4.5 ml. of pyridine was dissolved 300 mg. of VIc. The flask was cooled in an ice bath and 280 mg. of *p*-nitrobenzoyl chloride was added. The flask was kept for 17 hr. at room temperature. The reaction mixture was then poured into a mixture of ice and saturated sodium bicarbonate solution. After stirring for a few minutes a crystalline product formed. When all of the ice had melted the product was filtered by suction and washed with water. It was recrystallized from absolute methanol–chloroform to give 290 mg. (77% yield) of small white needles, m.p. 160–161.5°, $[\alpha]^{23}D$ −2.46° (*c* 8.14 $CHCl_3$).

Anal. Calcd. for $C_{41}H_{31}NO_{13}$: C, 66.03; H, 4.19; N, 1.88. Found: C, 65.87; H, 4.14; N, 1.91.

1-O-p-Nitrobenzoyl-2,3,5,6-tetra-O-benzoyl-D-talofuranose (VIId). A syrup (0.517 g.) containing approximately 0.419 g. of VId was dissolved in 9 ml. of pyridine, cooled to 0°, and 400 mg. of *p*-nitrobenzoyl chloride was added. After 21 hr. at room temperature the dark brown solution was poured into a mixture of ice and saturated sodium bicarbonate, and the mixture was stirred for 45 min. The product was extracted with chloroform, and the chloroform layer was washed with saturated sodium bicarbonate and water and dried over magnesium sulfate. The dark color was discharged by treatment with Norit A and filtration through a pad of Celite 535. The nearly colorless solution was evaporated to a syrup, and traces of pyridine were removed by addition and evaporation of toluene three times. The third time the syrup solidified. The solid mass was dissolved in a minimum amount of warm chloroform, and two volumes of warm absolute methanol were added. Crystallization occurred after the solution had cooled to room temperature. Recrystallization from methanol–chloroform afforded 140 mg. (27% yield) of product, m.p. 188–189.5°, $[\alpha]^{22}D$ −25.0° (*c* 5.39, $CHCl_3$).

Anal. Calcd. for $C_{41}H_{31}NO_{13}$: C, 66.03; H, 4.19; N, 1.88. Found: C, 66.03; H, 4.23; N, 1.83.

1-O-p-Nitrobenzoyl-2,3,5,6-tetra-O-benzoyl-D-altrofuranose (VIIe). In a manner similar to that for VIId, 4.8 g. of syrup containing approximately 4.1 g. of VId was treated with *p*-nitrobenzoyl chloride. After the work-up 1.08 g. (22% yield) of the product was obtained crystalline from warm absolute ethanol–chloroform. An analytical sample obtained by recrystallization from ethanol–chloroform gave clusters of tiny needles, m.p. 154–155°, $[\alpha]^{20}D$ −135.3° (*c* 4.02, $CHCl_3$).

Anal. Calcd. for $C_{41}H_{31}NO_{13}$: C, 66.03; H, 4.19; N, 1.88. Found: C, 66.13; H, 4.12; N, 1.96.

(22) C. S. Hudson and J. M. Johnson, *J. Am. Chem. Soc.*, **38**, 1223 (1916).