duced pressure and the resultant sirup was precipitated from a small volume of methanol by the addition of abs. ether; yield 1.82 g. This amorphous product was crystallized from methanol–chloroform; yield 1.50 g., m.p. 132–134°, $[\alpha]^{27}D$ −100° (*c* 1.9, water).

Anal. Calcd. for $C_{12}H_{23}O_{10}N_2(CH_3CO)$: C, 42.21; H, 6.58; N, 7.03; CH_3CO, 10.8. Found: C, 42.21; H, 6.91; N, 7.09; CH_3CO, 11.0.

Oxidation of 4-(N-Acetyl-2-amino-2-desoxy-D-galactopyranosyl)-L-gulonamide to 2-(N-Acetyl-2-amino-2-desoxy-D-galactopyranosyl)-D-erythruronamide (V).—An amount of 0.9987 g. (2.51 millimoles) of crystalline 4-(N-acetyl-2-amino-2-desoxy-D-galactopyranosyl)-L-gulonamide (IV) was oxidized at 12° in 100 ml. of solution with 5.28 millimoles of sodium metaperiodate. After 15 hr., titration of an aliquot showed that all of the periodate had been reduced. Thereupon ionic material was removed by successive passage of the solution over Amberlite[18] exchange resins (200 × 40 mm., diam.) IR-4 and IR-100 and the sirup obtained on solvent removal was crystallized from methanol by the addition of abs. ethanol. The crystals were dried under reduced pressure at 78°; yield 0.313 g., m.p. 177–179°, $[\alpha]^{27}D$ −77° (*c* 1.5, water).

Anal. Calcd. for $C_{10}H_{17}O_8N_2(CH_3CO)$: C, 42.86; H, 5.99; N, 8.33; CH_3CO, 12.8. Found: C, 42.87; H, 5.29; N, 8.08; CH_3CO, 13.1.

Periodate Oxidation of Sodium Chondroitinsulfate (Neutral Salt).—An amount of 2.01 g. (4.0 millimoles per disaccharide unit of calcd. 503 mol. wt.) of neutral sodium chondroitinsulfate (S, 6.01; $[\alpha]^{28}D$ −24°, *c* 2 in water) was oxidized at 26° in 100 ml. of solution with 7.92 millimoles of sodium metaperiodate. The initial *p*H was 5.5. Aliquots showed that slightly more than 1 mole (per disaccharide unit) of oxidant was consumed with the formation of small amounts (*ca.* 0.1 mole) of formic acid or 1.0 mole oxidant consumed at 60 hr. when corrected (decreased) for formic acid produced. At this point the excess periodate was destroyed by the addition of ethylene glycol, the solution was reduced in volume and treated with excess barium chloride. The precipitated barium iodate was removed by filtration and the organic material was precipitated in the filtrate by the successive addition of ethanol and ether. The filtered precipitate was dissolved in water and deionized by successive passage through Amberlite[18] IR-100 and IR-4 exchange resin columns (17.5 × 2.5 cm., diam.). The effluent was concentrated under reduced pressure to a sirup which was precipitated from a small amount of water by three volumes of ethanol. The precipitate was removed by filtration, washed with alcohol and ether and dried at room temperature in a vacuum desiccator. This product exhibited a negative Dische hexuronic acid color test[22] and a positive hexosamine color test.[23] It gave a negative sulfate test which became positive after acid hydrolysis. It is to be noted that iodate ion interferes with both of the color tests cited above by producing a green color in the Dische test when hexuronic acid is present and by preventing the formation of the pink color in the hexosamine test.

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[CONTRIBUTION FROM THE NORTHERN REGIONAL RESEARCH LABORATORY[1]]

N-Glycosyl Derivatives of Secondary Amines

BY JOHN E. HODGE AND CARL E. RIST

New data on the optical rotations of glycosyl derivatives of piperidine, diethanolamine and dibenzylamine are presented. The D-glucosyl derivatives of piperidine and diethanolamine do not show mutarotation in dry pyridine, whereas the D-galactosyl and D-mannosyl derivatives of piperidine do. Acid catalysts and alcoholic reaction media were found to be unnecessary in the preparation of N-glycosyl derivatives of strongly basic amines. Evidence is given to show that the compound heretofore known as N-D-glucosyldibenzylamine is actually a 1-desoxy-1-aminofructose (isoglucosamine) derivative.

Investigations of glycosylamines and amino-sugar reactions have increased in recent years because of results of research on nucleic acids, vitamins of the B-complex, coenzymes and intermediates in the non-enzymatic browning of foods. The lack of knowledge on the structural configuration of N-substituted glycosylamines, and particularly on their transformations in solution, has recently been discussed.[2a,3,4] Recent studies on the mutarotations of glycosylamines have been reported by Isbell and Frush[5] and by Pigman, Cleveland, Couch and Cleveland.[6] We have new data to report on the optical rotations of tertiary glycosylamines.

Kuhn and Birkofer,[7] because of their observations on the unexpected mutarotation of N-D-glucosylpiperidine and N-D-glucosyldibenzylamine in pyridine, formulated a theory of mutarotation,[2b,7b] in which they postulated quaternary base or salt formation as a requisite for the assumed Schiff base intermediate between anomeric α- and β-glycosidic forms. Our data show that N-D-glucosylpiperidine does not mutarotate in pyridine,[8] and the compound considered as N-D-glucosyldibenzylamine[7a] is actually a 1-desoxy-1-amino-D-fructose (isoglucosamine) derivative. These results indicate that more information on the optical rotations of tertiary glycosylamines is needed to confirm the theory.

In dry pyridine, a pure glycosyl derivative of a secondary amine should not show mutarotation through a Schiff base form, because protons would not be available for formation of the necessary cation. We have observed no mutarotation in dried pyridine for either N-D-glucosylpiperidine or N-D-glucosyldiethanolamine. On the other hand, we found that N-D-mannosylpiperidine and N-D-galactosylpiperidine do show mutarotation in dried pyridine. These mutarotations may not occur through the Schiff base form, however; they may occur by other intramolecular rearrangement. Evidence for a rearrangement of N-D-mannosylpiperidine in pyridine was noted when we failed to obtain an acetyl

(1) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

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(8) Two attempts to prepare Kuhn and Birkofer's mutarotating N-D-glucosylpiperidine of m.p. 115° resulted only in the initial formation of an impure product. After several recrystallizations the compound melted at 128–129° (dec.) and showed no mutarotation in pyridine.

derivative in pyridine–acetic anhydride at 0° under conditions which gave a nearly quantitative yield of N-(tetraacetyl-D-glucosyl)-piperidine from N-D-glucosylpiperidine. In the case of the mutarotating mannose derivative, browning discoloration occurred on acetylation, whereas none was noted for non-mutarotating N-D-glucosylpiperidine. The same type of browning was obtained in attempts to acetylate 1-desoxy-1-piperidino-D-fructose,[9] the Amadori rearrangement product of N-D-glucosylpiperidine, in pyridine–acetic anhydride.

In the preparation of glycosyl derivatives of highly basic amines, such as piperidine, *n*-butylamine and ethanolamine, we have found that no reaction medium or catalyst is necessary. Customarily, either an alcoholic medium[7a,10,11] or an acid catalyst[12,13] has been used with these amines.[6] The yields and ease of isolation of the product were improved in some cases by our procedure.

N-D-Glucosyldiethanolamine and its hexaacetate, N-1′-D-mannitylpiperidine and its pentaacetate, 1-desoxy-1-dibenzylamino-D-fructose, and the hydrochloride of N-D-glucosylpiperidine are reported here for the first time. The other glycosyl and glycitylamines (N-D-glucosylpiperidine, N-1′-D-sorbitylpiperidine and its pentaacetate, N-D-mannosylpiperidine, N-D-galactosylpiperidine and N-D-glucosylethanolamine) were studied and are reported because of meager or conflicting data in the literature.

Experimental[14]

The mutarotations of N-D-glucosylpiperidine hydrochloride, N-D-glucosylpiperidine, an equimolar mixture of D-glucose and piperidine, and N-D-glucosylethanolamine in water are shown in Fig. 1. N-D-Glucosylpiperidine hydrochloride (curve 1) gave only a rapid change in rotation to a constant value. Since the constant rotation reached is equal to that calculated from the D-glucose content of the solution, the mutarotation can be ascribed to hydrolysis. Crystalline N-D-glucosylpiperidine hydrochloride was hydrolyzed to D-glucose and piperidine hydrochloride on standing in ordinary moist air (see below).

With N-D-glucosylpiperidine, in contrast to the hydrochloride, the solution was alkaline (pH > 11), and degradation reactions occurred concurrently with hydrolysis. The specific rotation fell to 0 ± 1° (curve 2). After 12 hours, the mutarotation curve was identical with that of an equimolar solution of D-glucose and piperidine (curve 3). The same type of mutarotation was shown by N-D-glucosylethanolamine at lower pH (curve 4). D-Glucose in 0.05 *N* sodium hydroxide also showed mutarotation to approximately zero specific rotation,[15] (curve 6), although at a much slower rate than N-D-glucosylpiperidine. In equimolar sodium hydroxide, however, the change in rotation of D-glucose was much faster, and the time required to reach zero rotation was about equal to that of N-D-glucosylpiperidine or of an equimolar mixture of D-glucose and piperidine (curve 5). Cavalieri and Wolfrom[16] have shown the absorption spectra of N-D-glucosyl-*n*-butylamine at equilibrium in water (pH 11.6) to be essentially identical with that of D-glucose (0.5 *M*) in sodium hydroxide (0.5 *N*).

N-D-Glucosylpiperidine.—Finely powdered anhydrous D-glucose, 18.0 g. (0.10 mole) and piperidine (b.p. 106–107°), 17.0 g. (0.20 mole), were stirred together for a few minutes until heat was evolved. The flask was then warmed on a steam-bath at intervals to keep the temperature of the mixture in the range 70–80° until a clear, amber-colored sirup was obtained (15 minutes). Absolute methanol (25 ml.) and acetone (25 ml.) were then added, and the solution was filtered. To the filtrate was added acetone (225 ml.). After cooling 2 days at 0°, the crystals which had formed were filtered, washed with 1:4 methanol–acetone, and dried *in vacuo* over calcium chloride; yield 17.8 g.; m.p. 125–126° (dec.). A second crop of crystals, 3.0 g., m.p. 124–125° (dec.), was obtained from the mother liquor and washings. The total yield, 20.8 g. (84%), was recrystallized from 1:3 methanol–acetone (400 ml.), producing 11.9 g. (48%) of pure white needles, m.p. 130° (dec.) (*cf.* Weygand[12]); $[\alpha]^{21}D$ +8.5° (*c* 5.0, dry pyridine) with no mutarotation observed from 1.5 minutes to 24 hours after solution; $[\alpha]^{25}D$ +3° (*c* 2.0, absolute methanol). For the mutarotation in water, see Fig. 1.

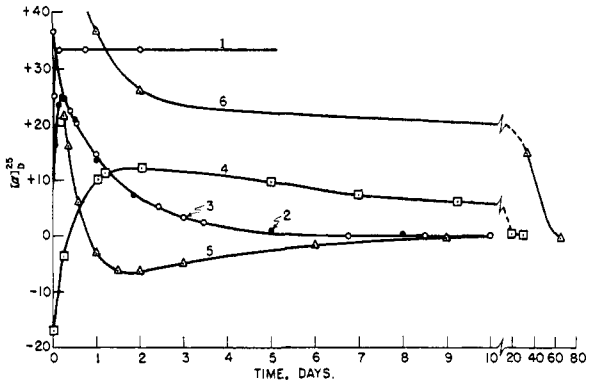

Fig. 1.—Mutarotations of aqueous solutions of (1) N-D-glucosylpiperidine hydrochloride, pH 6, *c* 2.0; (2) N-D-glucosylpiperidine, pH 11.5, *c* 4.0; (3) equimolar solution of D-glucose, *c* 2.3, and piperidine, pH 11.6; (4) N-D-glucosylethanolamine, pH 9.5, *c* 1.0; (5) equimolar solution of D-glucose, *c* 1.9, and sodium hydroxide, 0.1 *N*; (6) D-glucose, *c* 2.3, and sodium hydroxide, 0.05 *N* (data of H. Trey[15]).

Anal. Calcd. for $C_{11}H_{21}O_5N$: C, 53.4; H, 8.56; N, 5.66. Found: C, 53.5; H, 8.35; N, 5.64.

In parallel experiments, α-D-glucose and β-D-glucose were shaken with two molecular equivalents of piperidine at 30° for 3 days. The clear, yellow sirups were diluted with methanol and ether producing 70 and 83%, respectively, of the theoretical yields of N-D-glucosylpiperidine. Both products were identical with the preparation described above.

N-D-Glucosylpiperidine reduced hot Fehling solution strongly. In 0.1 *N* sodium hydroxide at 25° there was no reduction of dichlorophenolindophenol solution.

N-(2,3,4,6-Tetraacetyl-D-glucosyl)-piperidine.—N-D-Glucosylpiperidine, 9.5 g., was acetylated in 2:1 pyridine–acetic anhydride (75 ml.) at −17° (18 hours) and at 0° (3 days). After concentration of the solution *in vacuo* the crystalline acetate was isolated with 1:1 ether–petroleum ether; yield 15.2 g. (95%), m.p. 123°; $[\alpha]^{25}D$ −3.5° (*c* 5.0, chloroform).

Anal. Calcd. for $C_{11}H_{17}O_5N(COCH_3)_4$: N, 3.37; $COCH_3$, 41.5. Found: N, 3.45; $COCH_3$, 42.0.

This compound was identical in melting point with that obtained by Kuhn and Birkofer[7a] from their mutarotating N-D-glucosylpiperidine by acetylation in pyridine–acetic anhydride, and also with that obtained by Baker[17] from the interaction of 2,3,4,6-tetraacetyl-α-D-glucosyl bromide and piperidine. The optical rotation has not been previously reported. We treated 2,3,4,6-tetraacetyl-α-D-glucosyl bromide with piperidine at 0° and obtained an acetate identical with N-(2,3,4,6-tetraacetyl-D-glucosyl)-piperidine in m.p., mixed m.p., and specific rotation. Hence, barring the migration of acetyl groups, the ring form of N-D-glucosylpiperidine is pyranose (see following paragraph). Also, the anomeric form is probably beta. The high yield (95%) and purity (m.p. 123°) of the tetraacetate indicates that

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(14) All melting and boiling points are corrected.

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this N-D-glucosylpiperidine is not an equilibrium mixture of α and β forms, unless one form is present at equilibrium in concentration less than 5% of the total.

2,3,4,6-Tetraacetyl-β-D-glucose.—N-(2,3,4,6-Tetraacetyl-D-glucosyl)-piperidine provides an easily prepared starting material for the preparation of tetraacetyl-β-D-glucopyranose. N-(2,3,4,6-Tetraacetyl-D-glucosyl)-piperidine, 4.15 g. (10 millimoles), was suspended in 98 ml. of 0.102 *N* HCl (10 millimoles), and the suspension was held at 25° for 3 hours and at 80° for 1 hour until all the crystals dissolved; $[\alpha]^{25}D$ +56° (constant). After concentration of the solution *in vacuo* with the addition of acetone and ether, crystals of piperidine hydrochloride, 1.2 g. (98%), m.p. 245–246°, were isolated. The colorless ethereal filtrate on dilution with light petroleum ether and cooling at 0° gave 0.1 g. of colorless prismatic crystals, m.p. 130–137°, and 2.0 g. (52%), m.p. 109–112°. Recrystallization from ether gave 2,3,4,6-tetraacetyl-β-D-glucose, 1.2 g., m.p. 112–120°; $[\alpha]^{25}D$ +6° (7 min.) → +83° (*c* 3.3, 99% ethanol, with a trace of ammonia added).

Anal. Calcd. for $C_6H_8O_6(COCH_3)_4$: $COCH_3$, 49.4. Found: $COCH_3$, 49.2.

N-D-Glucosylpiperidine Hydrochloride.—N-D-Glucosylpiperidine, 5.0 g., was dissolved in 20 ml. of anhydrous methanol, and 9 ml. of 2.25 *N* HCl (one molecular equivalent) in methanol was added. On adding 100 ml. of acetone, crystallization began immediately; yield 5.6 g. (98%); white needles, m.p. 144° (with gas evolution); $[\alpha]^{21}D$ +4° (3 min.) → +33.5° (constant after 2 hours; *c* 2.0, water). The end rotation is equal to that calculated from the D-glucose content of the solution, assuming complete hydrolysis and $[\alpha]^{21}D$ +52.7° for D-glucose (see Fig. 1).

Anal. Calcd. for $C_{11}H_{22}O_5NCl$: N, 4.94; Cl, 12.50. Found: N, 4.78; Cl (ionic), 12.34.

A preparation of N-D-glucosylpiperidine hydrochloride of higher m.p. was obtained by deacetylating N-(2,3,4,6-tetraacetyl-D-glucosyl)-piperidine, 4.0 g., in 1.1 *N* HCl in methanol (20 ml.). After the solution had stood at 25° for 1 month, 1.5 g. (55%) of long needle crystals were obtained, m.p. 150–151° (dec.); $[\alpha]^{21}D$ −1° (3 min.) → +33.0° (constant from 2.5 to 24 hours; *c* 2.1, water). Found: Cl (ionic), 12.50.

After 6 months standing in a screw-capped vial, the crystals of N-D-glucosylpiperidine hydrochloride had coalesced to a colorless, partially crystalline sirup. Extraction of 2.6 g. of the sirup with absolute ethanol gave 1.6 g. (85%) of α-D-glucose, $[\alpha]^{25}D$ +109° → +52.7° (*c* 5, water), and piperidine hydrochloride, m.p. 245°.

N-D-Mannosylpiperidine.—By the procedure described for N-D-glucosylpiperidine, 72% of the theoretical amount of N-D-mannosylpiperidine, m.p. 115–116° (dec.), was obtained as fine, white needles, $[\alpha]^{24}D$ −21.6° (3 min.) → +13.5° (constant from 1 to 3 days; *c* 1.0, methanol) (*cf.* Hanaoka[10]). In dry pyridine, mutarotation was observed; $[\alpha]^{24}D$ −27.7° (2 min.) → +24.2° (constant from 1 to 3 days; *c* 2.0). The compound in 0.1 *N* sodium hydroxide did not reduce dichlorophenolindophenol solution.

Anal. Calcd. for $C_{11}H_{21}O_5N$: C, 53.4; H, 8.56; N, 5.66. Found: C, 53.3; H, 8.41; N, 5.69.

N-D-Galactosylpiperidine.—By the procedure described for N-D-glucosylpiperidine, 76% of the theoretical amount of N-D-galactosylpiperidine, m.p. 128–129° (dec.), was obtained as glittering platelets; $[\alpha]^{25}D$ + 14.4° (3 min.) → −3.6° (minimum, 1.5 through 4 hours) → 0.0° (26 hours; *c* 1.0, methanol). The compound is identical with that obtained by Hanaoka[10]; however, the optical rotation in pyridine has not been reported. We found mutarotation in dried pyridine: $[\alpha]^{25}D$ −10.2° (4 min.) → −20.7° (constant after 18 hours; *c* 2.0). The compound in 0.1 *N* sodium hydroxide at 25° did not reduce dichlorophenolindophenol solution.

N-D-Glucosyldiethanolamine.—Finely ground anhydrous D-glucose, 36 g. (0.20 mole), was stirred with diethanolamine (m.p. 25–26°), 34 g. (0.32 mole). After the mixture was warmed on the steam-bath for 10 minutes, absolute ethanol (50 ml.) was added and heating was continued for 40 minutes at 70–80°. The clear, yellow solution was diluted with 50 ml. of ethanol and filtered. Ether (50 ml.) was then added and, after seeding, the product crystallized slowly on standing at 0° for 24 hours. The crystals were filtered off, washed with ethanol, and dried *in vacuo* over calcium chloride; yield 31.5 g. (58%), dense prismatic needles, m.p. 123–124°. Recrystallization from 150 ml. of absolute methanol gave 22 g., m.p. 128°; $[\alpha]^{25}D$ −22.5°, without mutarotation in 7 hours (*c* 4.0, pyridine).

Anal. Calcd. for $C_{10}H_{21}O_7N$: C, 44.9; H, 7.92; N, 5.24. Found: C, 45.0; H, 7.99; N, 5.34.

Without the use of ethanol as a solvent, the yield was 68%, m.p. 121°. The product was generally insoluble in cold organic solvents, except pyridine. It was but slightly soluble in methanol at 25°, only slightly soluble in hot dioxane, and moderately soluble in hot alcohols. In 0.1 *N* sodium hydroxide at 25° it did not reduce dichlorophenolindophenol solution; it did reduce hot Fehling solution. This compound was more stable toward deterioration with browning in moist air than N-D-glucosylpiperidine.

Hexaacetyl-N-D-glucosyldiethanolamine.—N-D-Glucosyldiethanolamine, 0.90 g., in 20 ml. of pyridine was cooled to 0°, and 3 ml. of acetic anhydride was added. The clear solution was kept at 0° for 16 hours and at 25° for 6 hours. After several concentrations with the addition of ethanol, the crystalline product was isolated; yield 0.75 g. (43%), m.p. 71°. Recrystallization from ethanol gave 0.50 g., white needles, m.p. 71.5°; $[\alpha]^{25}D$ −48° (*c* 2.0, chloroform).

Anal. Calcd. for $C_{22}H_{33}O_{13}N$: N, 2.70; $COCH_3$, 49.7. Found: N, 2.71; $COCH_3$, 49.7.

N-D-Glucosylethanolamine.—This compound was prepared by Mohammad and Olcott[11] using ethanol as a reaction medium. Their yield was not stated and the product was difficult to isolate. In two experiments, without the use of a reaction medium (see N-D-glucosylpiperidine), we have obtained N-D-glucosylethanolamine in 83 and 91% yields; m.p. 114–116° (dec.); recrystallized from 1:1 methanol–acetone, m.p. 116° (dec.). The optical rotation has not been previously reported; $[\alpha]^{25}D$ −25.3° (12 to 25 min.) → +3.5° (constant from 3 to 5 days after dissolving; *c* 1.0, pyridine). The mutarotation in water is given in Fig. 1.

N-D-Glucosyl-*n*-butylamine.—To determine whether a catalyst is necessary in the preparation of glucosyl derivatives of strongly basic amines, the experiment of Mitts and Hixon[13] with *n*-butylamine was repeated without adding hydrochloric acid. The yield, 10.2 g., m.p. 88–89°, was virtually the same as that of Mitts and Hixon who obtained 11 g., m.p. 86–87°; hence, an acid catalyst is not necessary in this preparation.

N-1′-D-Mannitylpiperidine.—D-Mannose, 18.0 g. (0.1 mole), and piperidine, 12.9 g. (0.15 mole), were warmed in 25 ml. of methanol until all the sugar dissolved (5 min.). Methanol (75 ml.) was added, then the solution was filtered and poured into a steel hydrogenation bomb. Raney nickel catalyst (6 g.) was added and hydrogen was admitted to 1900 lb./sq. in. The bomb was heated at 70–80° for 4 hours with continuous rocking. The pale yellow solution obtained was filtered to remove the nickel and was then concentrated *in vacuo* to a crystalline residue. The product was recrystallized from absolute ethanol yielding 14.5 g. (58%) of cubic prisms, m.p. 143–144°. A second recrystallization gave the pure compound, m.p. 145°; $[\alpha]^{26}D$ −32.7° (*c* 4.0, pyridine).

Anal. Calcd. for $C_{11}H_{23}O_5N$: C, 53.0; H, 9.30. Found: C, 53.1; H, 9.32.

N-1′-D-Mannitylpiperidine crystallized in two different forms. The higher melting form, m.p. 145°, consisted of dense, nearly cubic prisms; whereas the lower melting form, m.p. 120–122° (with resolidification and final melting at 144°), consisted of thin, elongated flakes. Both forms showed the same specific rotation in pyridine, $[\alpha]^{25}D$ −32.7° (*c* 4.0), and the same carbon and hydrogen analysis. They also gave the same pentaacetyl derivative on acetylation in pyridine–acetic anhydride. N-1′-D-Mannitylpiperidine did not reduce hot Fehling solution.

Pentaacetyl-N-1′-D-mannitylpiperidine.—Dry pyridine (7 ml.) and acetic anhydride (3 ml.) were mixed, and N-1′-D-mannitylpiperidine, 1.0 g., was added. After standing at 25° for 18 hours the colorless solution was concentrated *in vacuo* to a clear, viscous sirup. On seeding with the pentaacetyl derivative [m.p. 54°, $[\alpha]^{25}D$ +39° (*c* 3.5, chloroform)] of the lower melting form of N-1′-D-mannitylpiperidine, the sirup crystallized and 1.9 g. of crude product was obtained. Recrystallized twice from petroleum ether, the yield was 1.4 g., m.p. 54–55°. Later, two recrystallizations from ether–petroleum ether gave the pure compound as large, elongated

prisms melting sharply at 77°; $[\alpha]^{25}D$ +38° (*c* 0.5, chloroform).

Anal. Calcd. for $C_{11}H_{18}O_5N(COCH_3)_5$: N, 3.05; $CO-CH_3$, 46.8. Found: N, 3.20; $COCH_3$, 46.3.

N-1′-D-Sorbitylpiperidine.—To identify our N-D-glucosylpiperidine further with that of Kuhn and Birkofer,[7a] we hydrogenated crystalline N-D-glucosylpiperidine (18.0 g.) under the conditions given for N-1′-D-mannitylpiperidine. The crude, crystalline product (17.7 g.) was recrystallized from 1:1 ethanol–ethyl acetate (50 ml.) yielding 15.1 g. (83%) of the glucamine derivative as white needles, m.p. 118–119°; $[\alpha]^{25}D$ −16.5° (*c* 4.0, pyridine). Kuhn and Birkofer[7b] reported m.p. 115–116°, $[\alpha]^{25}D$ −22° (*c* 0.55, pyridine). In water our preparation gave a *p*H 10.5 and a specific rotation of −17.7° at 25° (*c* 5.00). In water plus one equivalent of hydrochloric acid, the specific rotation was −31° at 25° (*p*H 6.0, *c* 1.00). In 20% acetic acid, $[\alpha]^{25}D$ −29.5° (*c* 12), unchanged on heating at 100° for 3 hours. The compound did not reduce hot Fehling solution.

Anal. Calcd. for $C_{11}H_{23}O_5N$: C, 53.0; H, 9.30; N, 5.62. Found: C, 52.9; H, 9.21; N, 5.70.

Pentaacetyl-N-1′-D-sorbitylpiperidine.—N-1′-D-Sorbitylpiperidine, 4.0 g., in a mixture of pyridine (18 ml.) and acetic–anhydride (10 ml.) was held at 0° for 3 hours and at 25° for 3 days. After repeated concentrations *in vacuo* with the addition of pyridine and ethanol, the yellow sirupy product was dried to constant weight, yield 6.9 g. (94%), b.p. 175–180° (0.5 mm.) (*cf.* Kuhn and Birkofer[7b]); recovery after distillation 6.8 g. (92%). The distillate was a colorless, viscous sirup, $[\alpha]^{25}D$ +19° (*c* 3.2, chloroform), which did not crystallize on long standing at 0° and 25°.

Anal. Calcd. for $C_{11}H_{18}O_5N(COCH_3)_5$: $COCH_3$, 46.8. Found: $COCH_3$, 46.6.

The Reaction of Dibenzylamine and D-Glucose; 1-Desoxy-1-dibenzylamino-D-fructose.—(a) Finely pulverized anhydrous D-glucose, 20 g., was mixed with absolute ethanol (50 ml.) and dibenzylamine, 30 g. (1.4 moles per mole D-glucose). The mixture was heated on the steam pot under reflux for 4 hours. After the first hour of heating, no color had developed and very little D-glucose had dissolved. Ammonium chloride, 1 g., was then added. The mixture became very dark on continued heating, yet the D-glucose did not dissolve completely. Finally, the mixture was filtered, removing unreacted D-glucose (4 g.). The crystals which formed in the filtrate were filtered, washed until white with ethanol, and dried; yield 6.5 g., white needles, m.p. 162° (dec.). From the mother liquor 2.2 g. more of the product was obtained; total yield 8.7 g. (27%, based on D-glucose dissolved). Recrystallization of the product from 60 parts ethanol gave no higher melting point; $[\alpha]^{25}D$ −89° (25 min.) → −35° (after 4 days; *c* 1.0, dry pyridine). Kuhn and Birkofer[7a] gave m.p. 159–160°, $[\alpha]^{21}D$ −88° (6 min.) → −40° (53.5 hours; *c* 0.55, pyridine).

Anal. Calcd. for $C_{20}H_{25}O_5N$: N, 3.90. Found: N, 3.85.

(b) Repeating the experiment (a), but without the addition of ammonium chloride and with heating for 1.5 hours only, 18% of the theoretical yield was obtained (based on D-glucose, 75%, dissolved). The product was identical to that described above.

The product was virtually insoluble in 0.1 *N* and 0.5 *N* sodium hydroxide at 25°; hence, the usual test for reducing power toward dichlorophenolindophenol[7a] was inconclusive. However, the product was sufficiently soluble in 0.1 *N* potassium hydroxide in methanol. In this alcoholic medium, dichlorophenolindophenol solution was decolorized at 25° in the manner of a 1-desoxy-1-aminofructose derivative. A parallel test with N-D-glucosylpiperidine in alcoholic potassium hydroxide gave no reduction of the dye. Other facts that indicated the product to be 1-desoxy-1-dibenzylamino - D - fructose, $(C_6H_5CH_2)_2N{\cdot}CH_2{\cdot}CO{\cdot}(CHOH)_3{\cdot}CH_2OH$, rather than a glucosylamine derivative, follow: (1) The crystals stood for several months in humid atmosphere without turning brown. (2) When subjected to conditions[9] known to produce the Amadori rearrangement in tertiary glucosylamines, there was no reaction; the crystals were recovered unchanged. (3) The crystals were dissolved in an excess of 1 *N* sulfuric acid and allowed to stand at 25° for 3 days. On neutralization with sodium hydroxide, the crystals were recovered unchanged. In another experiment the crystals were dissolved in one equivalent of hydrochloric acid, and the solution was heated at 85–90° for 2 hours. After the addition of sodium hydroxide equivalent to the acid added, 82% of the initial crystalline compound was recovered. (4) A compound identical with that described above was obtained by treating D-mannose with dibenzylamine under the new conditions[9] that produce the Amadori rearrangement.

1-Desoxy-1-dibenzylamino-D-fructose from D-Mannose.—D-Mannose, 2.25 g., and dibenzylamine, 4.1 g. (1.5 moles per mole of D-mannose), were warmed together on a steam-pot for 15 minutes. No reaction was apparent. A 1:1 solution of ethanol–ethyl malonate (10 ml.) was then added, and heating was continued for 30 minutes. The D-mannose dissolved after heating in the mixed solvent for 15 minutes, and the solution became progressively yellow, amber, then orange-colored. Crystallization occurred on cooling the mixture; yield 1.85 g. (60%); m.p. 161–162° (dec.). A mixed m.p. with the reaction product from D-glucose and dibenzylamine (m.p. 162°) was not depressed. The crystals in 0.1 *N* potassium hydroxide in methanol at 25° reduced dichlorophenolindophenol solution, $[\alpha]^{24}D$ −89° (15 min.) → −35° (after 7.5 days; *c* 0.76, pyridine).

Anal. Calcd. for $C_{20}H_{25}O_5N$: C, 66.8; H, 7.01; N, 3.90. Found: C, 66.7; H, 7.18; N, 3.88.

Hence, the compound known heretofore as dibenzylamine-N-glucoside[7] is doubtless 1-desoxy-1-dibenzylamino-D-fructose (N-dibenzyl-D-isoglucosamine). This is the first example of a non-aryl 1-desoxy-1-aminofructose derivative to be isolated and reported.[2b,13] Another example we have found is 1-desoxy-1-piperidino-D-fructose.[9] However, 5-trityl-1-desoxy-1-piperidino-D-xyloketose has been reported.[18] Two attempts to prepare true N-D-glucosyldibenzylamine were unsuccessful; only D-glucose and 1-desoxy-1-dibenzylamino-D-fructose were recovered.

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(18) K. Zeile and W. Kruckenberg, *Ber.*, **75**, 1127 (1942).