is much less than in the absence of silver nitrate, but is greater than corresponds to the amount of free butene. However, satisfactory rate constants were found when it was assumed that only the free butene present in the silver nitrate solution hydrates. The average value of the constants is greater than the known constant in the absence of silver ion. It is concluded that complexed butene does not hydrate.

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The Analysis of Gamma-Fructoside Mixtures by Means of Invertase. V. Methylated and Acetylated Derivatives of Crystalline α-Methyl- and α-Benzyl-fructofuranoside[1]

BY C. B. PURVES AND C. S. HUDSON

The products obtained by the action of chemical reagents on fructose are in most instances complex mixtures not easily separable into their constituents by crystallization or by other methods. This circumstance adds greatly to the experimental difficulty of studying the chemistry of the ketose and in consequence also adds to the value of the few crystalline derivatives which have been prepared from it. The very readily hydrolyzed or gamma-methylfructoside isolated two years ago[2b] was a pure crystalline individual[3] and therefore provided a welcome new starting material for such studies, some of which are recorded in this article.

When the highly dextrorotatory tetramethyl derivative of the glycoside was hydrolyzed with aqueous acid, the less dextrorotatory liquid product was found to be tetramethyl fructofuranose.[4] These facts proved that the "crystalline gamma-methylfructoside" or the "glycoside c" of earlier articles[2b,5a,5b] was in reality α-methylfructofuranoside. The methylation of this substance was not easy. Silver oxide and methyl iodide with anhydrous dioxane as an initial solvent yielded fully methylated products with low and variable specific rotations in water (112, 118°) even after the removal of the methylated methyl esters which they contained (up to 17.6%). Dipotassium and tetrapotassium derivatives reacted very slowly and incompletely with methyl iodide even in the absence of liquid ammonia.[6] The satisfactory methylations, carried out with the help of thallous ethylate by a special method adapted from the work of Menzies,[7] gave tetramethyl α-methylfructofuranoside as a mobile liquid free from esters and with a specific rotation of 129.4° in water. An interesting liquid dimethylfructose, whose optical rotation passed through a minimum near 10° and whose methoxyl groups perhaps occupied the 3,4 positions, was prepared from the corresponding dimethyl α-methylfuranoside. The latter was an intermediate product in the thallous ethylate methylations.

A brief search for derivatives of the glycoside which might be of use in its separation from mixtures resulted in the discovery of tetraacetyl α-methylfructofuranoside in the form of crystals melting at 48–48.5° and having a specific dextrorotation of 88.1° in chloroform. The first crystals were obtained after long delay by acetylating the carefully purified glycoside with Liebermann's reagents but were subsequently prepared from sucrose. The fructofuranoside failed to form a sparingly soluble derivative with barium hydroxide or methylate and yielded no crystalline addition compound with alcoholic potassium acetate.[8] When equimolecular amounts of α-methylfructofuranoside and of hydrogen chloride were mixed in concentrated anhydrous dioxane solution, however, a white, gelatinous carbohydrate–hydrogen chloride addition compound immediately separated and at once began to decompose to a dark, copper reducing tar. Although this ill-defined and highly unstable complex was of a type new to sugar chemistry, such compounds have been inferred to exist as transitory inter-

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

(2) Purves and Hudson, (a) THIS JOURNAL, **56**, 702 (1934); (b) **56**, 708 (1934).

(3) Melting at 80.5–81° and not at 69° as previously stated.

(4) Haworth, Hirst and Nicolson, *J. Chem. Soc.*, 1513 (1927).

(5) Purves, THIS JOURNAL, (a) **56**, 1969 (1934); (b) **56**, 1973 (1934).

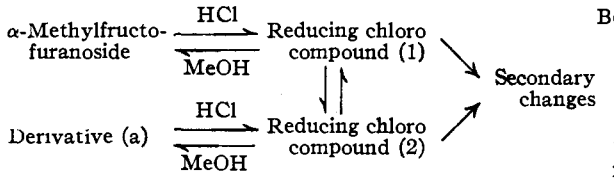
(6) Muskat, *ibid.*, **56**, 2449 (1934).

(7) Fear and Menzies, *J. Chem. Soc.*, 937 (1926).

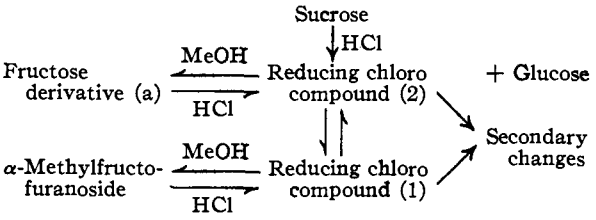
(8) *Cf.* Watters, Hockett and Hudson, THIS JOURNAL, **56**, 2199 (1934).

mediates in the transformations of glycosides dissolved in acid alcohols. Voss and Wachs[9] recently studied some aspects of the subject and discussed the relevant literature.

In the present case, no precipitate appeared when the dioxane solution was 0.0263 molar with respect to the glycoside and 0.025 normal with hydrogen chloride. The change with time both in the specific rotation (Fig. 1 Curve A) and in the copper reducing power of the solution (Fig. 1 Curve B) pointed to the occurrence of a complicated sequence of reactions. The maximum reduction attained, 49% of that theoretically possible, suggested that about half of the hydrogen chloride existed at this point as a copper-reducing chloro addition or substitution compound. After twenty-two hours at 20° almost half of the carbohydrate had been destroyed. The entire data supported the conclusion that a very rapid addition of hydrogen chloride to the fructofuranoside was followed by the formation of a highly unstable, copper reducing chloro compound. This partly decomposed and partly recombined with hydroxyl groups in the fructose molecule, thereby liberating hydrogen chloride which united with more of the glycosidic residues. These ideas supply an attractive explanation of the behavior of α-methylfructofuranoside in methyl alcoholic hydrogen chloride, when the starting material very rapidly attained an equilibrium with a second non-reducing gamma-fructose derivative (a) which was hydrolyzed by invertase[5a]

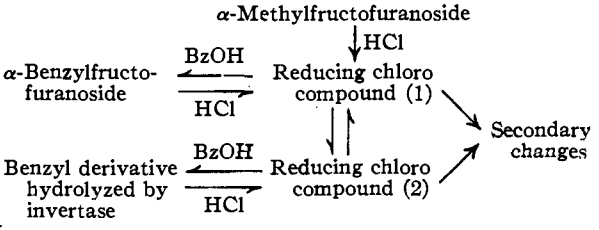


In this reaction the reduction was negligible throughout and the secondary changes were inappreciable for several hours. The concentration of intermediate chloro compounds was apparently restricted to a minute figure by an extremely rapid recombination with the large excess of methyl alcohol present. As shown in the scheme, this partial transformation of the glycoside suggested the nature of the primary equilibrium supposed to exist between the chloro compounds (1) and (2). Another example was drawn from the research already published[5b] concerning the scission of sucrose in methyl alcohol containing hydrogen chloride. The experimental data were consistent with the following set of reactions



A distinct optical exaltation was displayed by the sucrose–acid methyl alcoholic solution during the first few minutes. This was due possibly to the formation of a sucrose–hydrogen chloride addition compound.

If the above views on the mechanism of the interaction between α-methylfructofuranoside and methyl alcohol containing hydrogen chloride were correct, it was possible to use the fructoside in synthetical operations by substituting another hydroxylic compound for the methyl alcohol. Benzyl alcohol was chosen because it was expected to give crystalline derivatives of convenient solubility from which it might eventually be removed quantitatively, as toluene, by hydrogenation with palladium.[10] The following reactions were predicted in acid benzyl alcohol



The specific rotation of α-methylfructofuranoside in the new, acid solvent first decreased very rapidly and then much more slowly (Fig. 1, Curve C), the break in the curve (region C) signalizing the end of the primary change. The product isolated at this time included reducing substances (8 mol. % as fructose) and a new, non-reducing benzyl derivative (28 mol. %) which had a calculated specific levorotation of −27° in water and was hydrolyzed to fructose by the enzyme invertase. These two constituents were removed by a fermentation with yeast and α-benzylfructofuranoside (26.5 mol. %) was recovered as a crystalline tetraacetate from the unfermented portion of the product. By the end of the primary reaction, therefore, the origi-

(9) Voss and Wachs, *Ann.*, **522**, 240 (1936).

(10) Richtmyer, THIS JOURNAL, **56**, 1633 (1934).

nal gamma-methylglycoside had been largely replaced by a mixture of gamma-benzylglycosides.

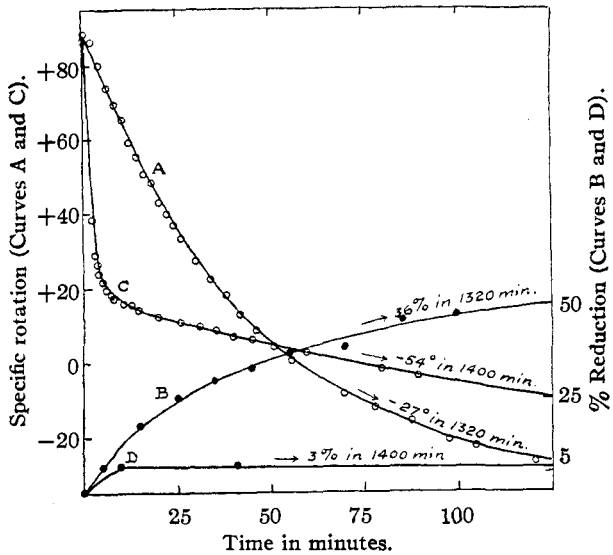


Fig. 1.—Action of hydrogen chloride on α-methylfructofuranoside: (A), specific rotation in dioxane; (B), copper reduction in dioxane; (C), specific rotation in benzyl alcohol; (D), copper reduction in benzyl alcohol.

The facts that the secondary optical change was fairly rapid and that a maximum copper reduction of 8 mol. % developed in the solution (Fig. 1, Curve D) suggested that labile chloro compounds accumulated as such in considerable amount and had time to undergo secondary transformations prior to recombination with the solvent.

Tetraacetyl α-benzylfructofuranoside was a beautifully crystalline substance melting at 84.5–85° and with a specific dextrorotation of 64.7° in chloroform. Deacetylation yielded α-benzylfructofuranoside as stout, rectangular tablets with a melting point of 89° and specific dextrorotations of 45.7 and 47.6° in water and dioxane, respectively. The new glycoside was hydrolyzed to fructose by aqueous acid 16.5 times more rapidly than sucrose but was unaffected by invertase or by yeast fermentation. When methylated with thallous ethylate it gave first a liquid dimethyl derivative and finally liquid tetramethyl α-benzylfructofuranoside with dextrorotations of 78.4° in dioxane and of 83.3° in chloroform. Scission of the latter with methyl alcoholic followed by aqueous hydrogen chloride resulted in an 80% yield of tetramethyl fructofuranose.[4] The isolation of the latter established the constitutions assigned to this series of benzyl derivatives.

The behavior of pure α-benzylfructofuranoside in benzyl alcoholic hydrogen chloride was similar to that of its methyl homolog in the same solvent. A very rapid primary decrease in specific rotation was followed by a fairly rapid secondary change (Fig. 2, Curve A) and was accompanied by the development of a substantial copper reduction (not plotted). The product isolated by arresting the reaction in the region A was submitted to the action of a powerful solution of invertase, which caused the copper reducing power of the mixture to increase from 12.4 mol. % to a final constant value of 44.8 mol. % as fructose. In Fig. 2, Curve C, the increase in the reduction at each time was plotted as a percentage of the total *enzymotic* increase, and from the curve the rate of hydrolysis was found to be about 5.1 times slower at each stage than the rate observed in an equivalent inversion of sucrose. A small initial exaltation in the optical rotatory power (Fig. 2, Curve B) paralleled the similar observation made during the partial hydrolysis of a gamma-methylfructoside mixture with invertase.[2a] The polarimetric and copper-reduction data enabled a specific levorotation of $-27 \pm 2°$ in water to be assigned to the non-reducing benzyl derivative unstable to the enzyme and the stable glycoside,

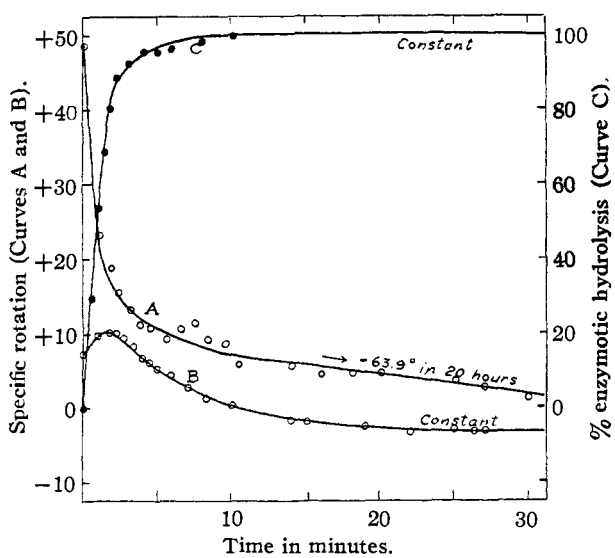


Fig. 2.—(A), Specific rotation of α-benzylfructofuranoside in acid benzyl alcohol; (B), hydrolysis of a gamma-benzyl fructoside mixture with invertase, specific rotation; (C), hydrolysis of the same gamma-benzy fructoside mixture with invertase, copper reduction, %.

with a dextrorotation of 41°, was mostly α-benzylfructofuranoside. The substrate hydrolyzed by

invertase consisted of the benzyl and fructoside radicals because these alone were present during its preparation and the calculation assumed it to be a true benzylfructoside of molecular weight 270.

Experimental

Sodium light and a saccharimeter with a conversion factor of 0.3462° circular = 1° V. were used in the optical observations, which were made at 20° in a 2-dm. tube unless otherwise stated. Copper reducing power was expressed throughout as fructose. Previous articles[2,8] stressed the necessity of employing redistilled, anhydrous, acid-free solvents and of avoiding elevated temperatures whenever possible in the preparative work. They also described the method adopted in making up solutions containing hydrogen chloride and gave details of the analytical technique.

Preparation of a Liquid Dimethyl α-Methylfructofuranoside.—Fifteen grams of the pure, recrystallized α-methylfructofuranoside, dissolved in 50 ml. of 100% ethyl alcohol, were shaken vigorously for a few seconds with 100 ml. of 1.615 *N* ethereal thallous ethylate[11] (2 equivalents). The round-bottomed flask used was then attached to a ground-in reflux condenser through the top of which the solvents were thoroughly removed, finally in high vacuum. Access of atmospheric carbon dioxide was minimized during these operations, and the temperature restricted to that of the room or less. The dithallium derivative remaining in the flask as a pale yellow, friable powder was incorporated with 100 ml. of ether containing 15 ml. of methyl iodide (50% excess) before the mixture was warmed under the reflux condenser for six hours, or until a sample was no longer alkaline to moist litmus paper. Sometimes it was necessary to renew the methyl iodide, and to continue the heating. Four 50-ml. portions of ether extracted the product from the insoluble thallous iodide and when the solvent was removed from the combined extracts, finally at 40° in high vacuum, a nearly quantitative yield of a liquid dimethyl α-methylfructofuranoside remained.

Anal. Calcd. for dimethyl methylfructoside, $C_9H_{18}O_6$: C, 48.7; H, 8.1; OCH_3, 41.9. Found: C, 48.5; H, 8.3; OCH_3, 41.5.

The colorless dimethyl methylglycoside had a refractive index of $n^{20}D$ 1.4632 and the following specific dextrorotations: in chloroform, +94.0° (*C*, 1.565; V., +8.50°); in water, +111.4° (*C*, 1.6; V., +10.30°); in dioxane, +95.3° (*C*, 1.508; V., +8.30°). The aqueous solution was quite clear.

A Liquid Dimethyl Fructose.—A solution containing 3.78 g. of the above dimethyl methylglycoside in 0.1 *N* hydrochloric acid was hydrolyzed completely by fifteen minutes of heating at 100°. The product, 3.6 g., isolated by standard methods, had a refractive index of $n^{19}D$ 1.4768 and a methoxyl content of 29.3% (calcd. for dimethyl fructose, $C_8H_{16}O_6$: OCH_3, 29.8%). A 2.061% aqueous solution had a levorotation of −1.30° V. five minutes after solution, changing to a final constant value of −2.05° V. within two hours. These data corresponded to a mutarotation from $[\alpha]^{20}D$ −10.9° to $[\alpha]^{20}D$ −17.2°. At temperatures of 4, 10, 17, 30 and 45° the same solution displayed specific rotations of −16.8, −18.9, −18.1, −15.5 and −11.3°, respectively. The rotation therefore passed through a minimum in the neighborhood of 10°.

Tetramethyl α-Methylfructofuranoside.—The methylation of the dimethyl α-methyl derivative, 12.63 g., was carried out with 2 equivalents of ethereal thallous ethylate and 2.7 mols of methyl iodide in the way already described. Ether, 100 ml., was used in place of absolute alcohol as the initial solvent. The reaction was not quite complete (found: OCH_3, 58.0%) and a single treatment with silver oxide and methyl iodide was necessary before the product was distilled with high vacuum into a very well cooled receiver. The yield was 11.68 g. with a refractive index of $n^{20}D$ 1.4417 which was identical with that of the last drop.

Anal. Calcd. for tetramethyl methylfructoside, $C_{11}H_{22}O_6$: C, 52.8; H, 8.8; OCH_3, 62.0. Found: C, 52.9; H, 8.9; OCH_3, 61.4.

Tetramethyl α-methylfructofuranoside was a mobile, colorless liquid which gave a clear aqueous solution taking up no alkali and therefore containing no esters. Its specific dextrorotation was: +115.9° in chloroform (*C*, 2.279; V., +15.26°); +113.1° in dioxane (*C*, 2.120; V., +13.85°); and +129.4° in water (C, 2.6; V., +19.45°).

The methylated fructofuranoside, 4.45 g., was hydrolyzed and the tetramethyl fructofuranose produced was isolated and distilled by standard methods; yield 3.88 g. or 92%.

Anal. Calcd. for tetramethylfructose, $C_{10}H_{20}O_6$: C, 50.9; H, 8.5; OCH_3, 52.5. Found: C, 50.9; H, 8.7; OCH_3, 51.9.

Its refractive index, $n^{20}D$ 1.4517, and specific rotation in water, +28.1° initially to +29.8° finally, were in agreement with the accepted constants for this compound ($n^{13}D$ 1.4513; $[\alpha]D$ +31.3°).[4]

Preparation of Tetraacetyl α-Methylfructofuranoside from Sucrose.—A fermented, aqueous solution of α-methylfructofuranoside contaminated with glucofuranosides was prepared from 180 g. of sucrose by the method already published.[5b] A cautious evaporation of the neutralized solution (*p*H 8) without the addition of butyl alcohol left 65 g. of a thick sirup. This was acetylated by shaking at room temperature with 20 g. of anhydrous sodium acetate and 320 ml. of acetic anhydride and by heating the resulting solution for ninety minutes on the steam-bath. The water-soluble product, recovered by standard methods in a total of 600 ml. of neutral, dry benzene, was a thick, orange colored sirup weighing 100 g. Crude, nearly colorless tetraacetyl α-methylfructofuranoside, 92 g., passed into the receiver when this sirup was fractionated in high vacuum; bath 200–230°. A more accurate fractionation than that carried out would probably have rendered the following crystallization less difficult. Two volumes of water were added to one volume of a 20% solution of the distillate in methyl alcohol, the solution was cooled until it was definitely opalescent and the clear supernatant liquid was copiously nucleated in a separate vessel which was kept for three days at 0–5°; yield 35 g., increased to 40 g. by working up and redistilling the mother liquors and residues. A similar but easy re-

(11) Menzies, *J. Chem. Soc.*, 1571 (1930). Crude, moist thallous hydroxide was first prepared by adding the equivalent of baryta to a hot 15% thallous sulfate solution and by cautiously evaporating the filtrate.

crystallization left 36 g. or 38% of the calculated amount of the product in a pure condition. The sample for the rotations and analyses was dried in a vacuum over soda lime.

Anal. Calcd. for tetraacetyl methylfructoside, $C_{15}H_{22}O_{10}$: C, 49.7; H, 6.1; OCH_3, 8.6. Found: C, 49.5; H, 6.1; OCH_3, 8.6, 8.5.

In an acetyl estimation (Kunz' method)[12] 0.2043 g. required 22.6 ml. of 0.1 *N* alkali; calcd. 22.6 ml. The deacetylation of 2.64 g. by 100 ml. of anhydrous, 0.00068 normal methyl alcoholic barium methylate left 1.38 g. of pure α-methylfructofuranoside, with the correct specific rotation of +91.7° in methyl alcohol; calcd. 1.416 g.

The matted fine needles or large, well-built stout prisms of tetraacetyl α-methylfructofuranoside melted at 48–48.5°, dissolved in water and petroleum ether and were very soluble in the other common organic solvents. The compound had the following specific dextrorotations observed at 19°: +88.1° in chloroform (*C*, 4; V., +20.35°); +84.4° in dioxane (*C*, 4; V., +19.50°); +91.3° in methyl alcohol (*C*, 2.069; V., +10.92°); and +84.0° in water (*C*, 1; V., +9.70° observed in a 4-dm. tube).

The Carbohydrate–Hydrogen Chloride Addition Compound.—A 12.76% solution of α-methylfructofuranoside in warm dioxane was cooled to room temperature before 10 ml. was mixed quickly with 2 ml. of dioxane made 2.63 *N* with hydrogen chloride. The mixture was therefore 0.526 *M* with respect to both constituents. The white gelatinous fluid rapidly darkened in color as a difficult filtration gave a colorless filtrate the first portion of which, 4.7 ml., was diluted immediately to 25 ml. with water and analyzed. Found in the dioxane filtrate: HCl, 0.106 *M* by titration, 0.106 *M* as silver chloride; copper reduction as fructose, 0.038 *M*, increased to 0.052 *M* by a Herzfeld hydrolysis. By difference, the precipitate contained carbohydrate and hydrogen chloride in the molar ratio of 0.474:0.420 or of 1.13:1. The apparent deviation from an exact equimolecular ratio was probably due to the destruction of fructose in the filtrate prior to dilution with water.

Behavior of α-Methylfructofuranoside in Dioxane Containing Hydrogen Chloride.—The solution described in the caption to Table I was prepared and examined by usual methods. After 5, 15, 25, 35, 45, 55, 70, 85, 100, 125, 150, 175, 204 and 1320 minutes its copper reducing power was 6.3, 18.0, 25.4, 30.0, 33.8, 37.4, 39.1, 47.6, 48.6, 50.7, 47.6, 50.7, 47.6 and 36.0%, respectively, of the maximum possible (Fig. 1, Curve B). After 1320 minutes only 52.8% of the original fructose was estimated in a Herzfeld hydrolysis. The polarimetric observations given in Table I were made in a 4-dm. tube.

Action of Anhydrous Benzyl Alcoholic Hydrogen Chloride on α-Methylfructofuranoside.—Samples, 0.5 ml., of the solution described in the caption to Table II were prepared for the estimations of copper reducing power by discharge into 50-ml. volumes of 0.0003 *N* aqueous caustic soda containing 3% of methyl alcohol. After 0, 9.5, 41, 134, 204, 366, 488 and 1400 minutes these reductions were 0.0, 6.9, 7.9, 6.4, 5.9, 4.8, 4.6 and 3.0%, respectively, of the maximum calculated from the fructoside present (see Fig. 1, Curve D). The specific rotations in Table II were calculated as due throughout to methyl glycoside.

(12) Kunz and Hudson, THIS JOURNAL, **48**, 1982 (1926).

TABLE I

OPTICAL ROTATION OF 0.0263 *M* α-METHYLFRUCTOFURANOSIDE IN DIOXANE 0.025 *N* WITH HYDROGEN CHLORIDE AT 18°[a]

Min.	V.° (L = 4)	$[\alpha]^{18}D$	Min.	V.° (L = 4)	$[\alpha]^{18}D$
0	+5.24	88.8[b]	38	1.07	18.1
2	5.10	86.4	42	0.77	13.0
4	4.73	80.2	46	.52	8.7
6	4.38	74.2	51	+ .27	+ 4.6
8	4.10	69.5	56	+ .05	+ 0.8
10	3.88	65.8	71	− .51	− 8.6
12	3.50	59.3	78	− .71	−12.0
14	3.28	55.6	88	− .97	−16.4
16	3.01	51.0	98	−1.22	−20.7
18	2.82	47.8	105	−1.31	−22.2
20	2.58	43.7	121	−1.55	−26.3
22	2.37	40.2	145	−1.78	−30.3
24	2.19	37.1	204	−2.10	−35.6
26	2.00	33.9	280	−2.25	−38.1
30	1.63	27.6	1320	−1.6	−27.1[c]
34	1.33	22.5			

[a] See Fig. 1, Curve A. [b] Separately observed in acid-free solvent. [c] Discoloration.

TABLE II

OPTICAL ROTATION OF A 7.8017% SOLUTION OF α-METHYLFRUCTOFURANOSIDE IN 0.03 *N* BENZYL ALCOHOLIC HYDROGEN CHLORIDE AT 20°[a]

Min.	V.°, obsd.	$[\alpha]^{20}D$	Min.	V.°, obsd.	$[\alpha]^{20}D$
0	+39.46	+87.6[b]	30	4.45	9.9
2.4	17.25	38.3	35	+ 3.85	+ 8.5
3.2	13.10	29.1	40	+ 3.25	+ 7.2
3.75	11.70	26.0	45	+ 2.70	+ 6.0
4.3	10.70	23.8	60	+ 1.15	+ 2.6
5.25	9.65	21.4	80	− 0.65	− 1.4
6.2	8.75	19.4	90	− 1.50	− 3.3
7.2	8.12	18.0	132	− 4.75	−10.5
8.0	7.75	17.2	180	− 8.25	−17.3
10.5	7.09	15.7	210	−10.05	−22.3
12.5	6.85	15.2	340	−16.85	−37.4
15.0	6.40	14.2	486	−21.10	−46.8
20	5.70	12.7	1140	−24.53	−54.4[c]
25.4	5.00	11.1	1395	−24.10	−53.5

[a] See Fig. 1, Curve C. [b] See Table I, note [b]. [c] $[\alpha]^{20}D$ −39.1° calcd. as benzyl rather than as methylfructoside.

Preparation of Tetraacetyl α-Benzyl- from α-Methylfructofuranoside.—Ten grams of the finely divided methyl glycoside dissolved almost entirely when vigorously shaken for six minutes at 20° with 100 ml. of benzyl alcohol made 0.03 *N* with hydrogen chloride gas. After six minutes, the acid was neutralized quickly and completely with 2 g. of silver oxide and the pale yellow, silver-free filtrate was diluted with 200 ml. of benzene and 800 ml. of light petroleum. This dilution made it possible to recover 94% of the product from the mixed solvents by three extractions with 100 ml. volumes of water. The combined aqueous extracts were shaken once with ether and prepared for fermentation. Analysis: reduction 0.208%, increased to 0.900% by invertase and to 2.50% by a Herzfeld hydrolysis. Starch-free yeast, 1 g., fermented two components of the mixture and left unfermented 7.92 g. of gamma-benzyl

fructosides with a specific dextrorotation of 46.2° in water. Cold pyridine, 50 ml., and acetic anhydride, 50 ml., acetylated this sirup overnight. A recrystallization of the product from ether yielded 6.9 g. of sticky crystals with a specific rotation of +64.4° in methyl alcohol. A final recrystallization from 20 ml. of methyl alcohol gave 6.0 g. of pure tetraacetyl α-benzylfructofuranoside, corresponding to 26.5% of the methylfructoside used.

Anal. (Sample dried at 0.1 mm. and 55° for ten hours.) Calcd. for tetraacetyl benzylfructoside, $C_{21}H_{26}O_{10}$: C, 57.5; H, 5.9. Found: C, 57.4; H, 5.9. In an acetyl estimation, 0.2822 g. took 25.9 ml. of 0.1 *N* alkali. Calcd. for four acetyl groups, 25.8 ml.

The glycoside melted sharply at 84.5–85°, was insoluble in water, sparingly soluble in petroleum ether and soluble in other organic solvents. It separated from ether or hot methyl alcohol as stout flat prisms and occasionally as clusters of long needles from a cold dilute solution of the latter solvent. The following specific dextrorotations refer to 4% solutions: in methyl alcohol, +65.65° (V., +15.17°); in chloroform, +64.7° (V., +14.95°) and in dioxane +58.42° (V., +13.50°).

Preparation of α-Benzylfructofuranoside from its Tetraacetate.—Absolute barium methylate, 1.5 ml. of 2 *N*, added to 20 g. of the pure tetraacetate dissolved in 400 ml. of ice-cold, anhydrous methyl alcohol, was just sufficient to render the mixture definitely alkaline to phenol red. After standing overnight at 0°, the faintly yellow solution was evaporated at 0° (30 mm.) to a thick sirup which still contained the trace of unneutralized barium. This was removed by diluting the sirup with 400 ml. of boiling ether and filtering the warm solution through absorbent carbon. The filtrate quickly deposited 9.6 g. of stout, well-built rectangular tablets which adhered to the bottom and sides of the beaker. A further 0.9 g. obtained from the concentrated mother liquor brought the total yield of α-benzylfructofuranoside up to 85% of the theoretical.

Anal. Calcd. for a benzylfructoside, $C_{13}H_{18}O_6$: C, 57.8; H, 6.7. Found: C, 58.0; H, 6.8. A 1.50% solution in 0.25 *N* aqueous acid at 20° had, after complete hydrolysis, a reduction of 0.98% and a levorotation of −5.35°. Calcd. for fructose 1.00% and −5.34° V.

The compound was quite pure when isolated because fractional recrystallizations made by adding ether to a concentrated dioxane solution failed to change the following constants: melting point, 89°; specific dextrorotation in dioxane, +47.60° (*C*, 2; V., +5.50°) and in water, +45.70° (*C*, 2.5; V., +6.60°). α-Benzylfructofuranoside was almost insoluble in petroleum ether, was soluble in benzene and ether and dissolved freely in alcohols, water, and dioxane. Its reduction of the Shaffer–Hartmann alkaline copper reagent was inappreciable. A 1.25% solution of the benzyl gamma-fructoside in 1% aqueous acid sodium phosphate was mixed with a powerful invertase preparation. After twenty hours the mixture still inverted added sucrose rapidly but retained the original rotation and a zero reduction in measurements precise enough to have detected a hydrolysis of 2% with ease. Invertase therefore neither hydrolyzed the glycoside nor was inactivated by it.

Hydrolysis of α-Benzylfructofuranoside by Aqueous Acid.—The changes in the rotation and copper reducing power of a 1.5% solution in 0.25 *N* hydrochloric acid at 20° were followed as described in the case of the α-methyl glycoside.[5a] A unimolecular velocity constant of 10^4K = 72 ± 1 (in minutes and decimal logarithms), calculated from reduction data ranging from 8 to 92% hydrolysis, showed the hydrolysis to be 16.5 times more rapid than that determined for sucrose in the equivalent conditions (10^4K for sucrose = 4.3 ± 0.04). The optical observations simultaneously made on the α-benzylfructofuranoside solution corresponded to unimolecular coefficients which rose uniformly from 10^4K = 65.2 (4.5% Hy.) to 10^4K = 76.8 (13.8% Hy.). They then diminished steadily to 10^4K = 66.3 ± 1 (66.4–95.7% Hy.).

A Liquid Dimethyl α-Benzylfructofuranoside.—Four grams of the pure benzyl glycoside, m. p. 89°, dissolved at room temperature in 25 ml. of 100% ethyl alcohol, gave an immediate, amorphous, pale yellow precipitate of the dithallium derivative when 18.5 ml. of 1.66 *N* ethereal thallous ethylate was added (2 equivalents + 4% excess). The methylation was completed as in the case of the α-methyl glycoside and a nearly theoretical yield of a viscid, dimethyl α-benzylfructofuranoside, $n^{19}D$ 1.5145, was isolated.

Anal. (Sample heated at 30° in high vacuum.) Calcd. for a dimethyl benzylfructoside, $C_{15}H_{22}O_6$: C, 60.4; H, 7.4; OCH_3, 20.8. Found: C, 60.2; H, 7.6; OCH_3, 21.0.

The substance had a specific dextrorotation of $[\alpha]^{19}D$ +57.1° in dioxane (*C*, 1.243; V., +2.05°; L = 1).

Tetramethyl α-Benzylfructofuranoside.—The dithallium derivative of the above dimethyl α-benzyl glycoside was prepared as an amorphous white precipitate by adding 2.1 equivalents of ethereal thallous ethylate to 4.1 g. dissolved in 30 ml. of ether. After methylation the product was remethylated with 7 g. of silver oxide and 4 ml. of methyl iodide. Tetramethyl α-benzylfructofuranoside (yield 88%) was a somewhat viscid liquid with a refractive index of $n^{19}D$ 1.4900 after drying at 35° in a high vacuum.

Anal. Calcd. for tetramethyl benzylfructoside, $C_{17}H_{26}O_6$: C, 62.5; H, 8.0; OCH_3, 38.0. Found: C, 62.5; H, 8.2; OCH_3, 38.2. *Subs.* 0.1215 g. took 0.0 ml. of 0.1 *N* alkali so that esters were absent.

The substance had specific dextrorotations at 19° of +78.4° in dioxane (*C*, 2.134; V., +9.67°), of +83.3° in chloroform (*C*, 2.162; V., +10.40°) and of +78.8° in methyl alcohol (*C*, 1.29; V., +5.87°). It was insoluble in water but dissolved readily in organic solvents.

Hydrolysis of Tetramethyl α-Benzylfructofuranoside.—The benzyl group of the water-insoluble glycoside was first replaced by the methoxyl radical by solution (3.1 g.) in 72 ml. of 0.03 *N* methyl alcoholic hydrogen chloride at 19°. Fifteen hours later, when the specific rotation had diminished to a steady dextro value of 33.7°, calculated as benzyl fructoside, the resultant mixture of water-soluble tetramethyl gamma-methylfructosides and benzyl alcohol was isolated and hydrolyzed by aqueous acid in the usual way. Ether, 50 ml., extracted most of the benzyl alcohol (and 5% of the product) from the neutralized hydrolysate (80 ml.) and chloroform subsequently extracted crude tetramethyl fructofuranose; yield 91.3% after distillation. The product still contained some benzyl alcohol (found, OCH_3, 46.4%; $n^{19}D$ 1.4585) and was fractionated in high vacuum. The first fraction containing the alcohol was re-

jected (0.70 g.; $n^{20}D$ 1.4735) and the second fraction was practically pure tetramethyl fructofuranose (1.23 g. or 49%).

Anal. Calcd. for tetramethyl fructose, $C_{10}H_{20}O_6$: C, 50.9; H, 8.5; OCH_3, 52.5. Found: C, 51.0; H, 8.6; OCH_3, 50.3.

The refractive index and the specific rotation in water, $n^{19}D$ 1.4508 and $[\alpha]^{20}D$ +29.8° (final value), respectively, were in good agreement with the constants accepted for tetramethyl fructofuranose ($n^{18}D$ 1.4513, $[\alpha]D$ +31.3°).[4]

Behavior of α-Benzylfructofuranoside in Benzyl Alcoholic Hydrogen Chloride.—After 0, 1.3, 2, 2.5, 12.7, and 1560 minutes the copper reducing power of the solution described in the caption to Table III was 0, 4.4, 6.5, 7.8, 22.1 and 5.1%, respectively, of the maximum possible from the fructose glycoside present. These reductions were determined by discharging 0.5-ml. samples into Shaffer–Hartmann boiling tubes each containing 1 ml. of a mixture of purified dioxane (5 parts) and 0.1 *N* aqueous caustic soda (1 part). Water, 3.5 ml., was added to each before the estimation, which was of less than usual accuracy. A 1-dm. polarimeter tube was used in the optical observations.

TABLE III

OPTICAL ROTATION OF A 2.25% SOLUTION OF α-BENZYL-FRUCTOFURANOSIDE DISSOLVED IN 0.03 *N* BENZYL ALCOHOLIC HYDROGEN CHLORIDE AT 20°[a]

Min.	V.°, obsd.	$[\alpha]^{20}D$	Min.	V.°, obsd.	$[\alpha]^{20}D$
0	+3.15	+48.5[b]	23	0.30	4.6
1	1.51	23.2	25	.23	3.5
1.75	1.22	18.8	27	.18	2.8
2.3	1.09	15.5	30	.08	1.2
3.2	0.87	13.4	35	.00	0.0
3.75	.72	11.1	40	− .10	− 1.5
4.5	.70	10.8	45	− .19	− 2.9
5.5	.60	9.2	55	− .40	− 6.2
6.5	.70	10.8	70	− .65	−10.0
7.5	.75	11.6	90.2	− .92	−14.2
8.3	.60	9.2	113	−1.31	−20.2
9.5	.55	8.5	144	−1.72	−26.5
10.3	.53	8.2	180	−2.22	−33.5
14	.37	5.7	270	−2.93	−44.4
16	.29	4.5	465	−3.87	−59.6
18	.30	4.6	1200	−4.15	−63.9
20	.30	4.6	1500	−4.05	−62.3

[a] See Fig. 2, Curve A. [b] See Table I, note *b*.

Partial Hydrolysis of a Benzyl-furanoside Mixture with Invertase.—A solution consisting of 2.00 g. of α-benzylfructofuranoside dissolved in 25 ml. of anhydrous 0.01 *N* benzyl alcoholic hydrogen chloride was observed at 23° for twelve minutes on the saccharimeter or until its specific dextrorotation had decreased to +9.5° (Fig. 2, Curve A, region A). The acid was neutralized thoroughly with silver oxide after fourteen minutes, and the product recovered in 40 ml. of water containing 4 ml. of 2% sodium hydrogen phosphate.[13] This faintly acid solution (*p*H 4.5) had an observed dextrorotation of +1.98° and a copper reduction of 0.392%, increased to 3.15% by a Herzfeld hydrolysis. These values were unchanged after twenty hours at 23°. An equal volume of powerful invertase solution was then added and the consequent changes in optical rotation observed in a 4-dm. tube (Table IV). The specific rotations were calculated as entirely due to [(3.15/2) × (3/2)] or 2.36% of benzylfructoside and the increase in the copper reductions was expressed as a percentage of the maximum hydrolysis *caused by the enzyme*. After 0.5, 1, 1.4, 1.75, 2.25, 3, 4, 5, 6, 8 and 10 minutes the hydrolysis was 29.6, 53.8, 68.9, 80.9, 88.7, 92.2, 95.5, 95.5, 96.7, 98.4 and 100%, respectively (Fig. 2, Curve C). The corresponding velocity coefficients, calculated for a unimolecular reaction, increased from 10^4K = 50.8 (0.5 min.) to 10^4K = 70.1 (2.25 min.) and subsequently diminished.[13]

(13) See preparation of tetraacetyl α-benzyl- from α-methylfructofuranoside.

TABLE IV

PARTIAL ENZYMOTIC HYDROLYSIS OF A GAMMA-BENZYL FRUCTOSIDE MIXTURE. OPTICAL ROTATIONS AT 23°[a]

Min.	V.°, obsd.	$[\alpha]^{23}D$	Min.	V.°, obsd.	$[\alpha]^{23}D$
0	+1.98[b]	+7.3	8.2	0.36	1.3
1	2.71	9.9	10	+ .06	+0.2
1.7	2.76	10.1	14	− .43	−1.6
2.2	2.76	10.1	15	− .50	−1.9
2.7	2.58	9.5	19	− .69	−2.5
3.3	2.26	8.3	22	− .86	−3.1
4	1.96	6.9	25	− .79	−2.9
4.4	1.68	6.1	26.3	− .84	−3.1
5	1.48	5.4	27	− .84	−3.1
5.7	1.16	4.3	35	− .89	−3.3
7	0.73	2.7	1200[c]	− .87	−3.2

[a] See Fig. 2, Curve B. [b] Observed separately in absence of enzyme. [c] The solution had an acidity of *p*H 4.4 and the enzyme still actively hydrolyzed added sucrose.

Specific Rotations of the Benzyl Derivatives Hydrolyzed and Unhydrolyzed by Invertase.—The initial solution after dilution with an equal volume of enzyme had a dextrorotation of +1.98° in a 4-dm. tube and a reduction of 0.195% as fructose. At the end of the enzymotic hydrolysis the levorotation was −0.87°, observed in a 4-dm. tube, and the corresponding reduction was 0.705%. Further hydrolysis with 0.33 *N* hydrochloric acid at 23° reduced the rotation to −16.49° (L = 4) and increased the reduction to 1.575%, corresponding to a correct specific rotation of −90.6° for the fructose produced. These data, in conjunction with the fact that a 1% solution of the ketose in water at 23° had a levorotation of −10.40° (L = 4), made it possible to calculate[2a] that the specific rotation of the benzyl derivative hydrolyzed by invertase was −27.7° in water while a rotation of +41.0° could be assigned to the non-reducing benzylfructofuranosides stable to the enzyme. These specific rotations were found to be −27.4° and +40.0°, respectively, in an independent experiment carried out at 20°.

The molar composition of the gamma-benzyl fructoside mixture isolated from the acid benzyl alcohol near point A (Fig. 2, Curve A) was also calculated to be approximately: fructose in a reducing condition, 12.4%; non-reducing derivative hydrolyzed by invertase, 32.4% and non-reducing derivatives stable to invertase, 55.2%. The derivative hydrolyzed by invertase was 0.0283 molar in the solution examined.

Comparative Enzymotic Hydrolysis of Sucrose.—The same invertase solution as used above was mixed at 23°

with an equal volume of an aqueous 1.938% sucrose solution carefully buffered to pH 4.4. The copper reduction of the resulting 0.0283 M mixture was plotted against time and the unimolecular velocity constants were calculated for 30, 40, 50, 60, 70, 80, and 90% inversion. These constants were, respectively, 5.31, 5.50, 5.31, 4.89, 4.74, 4.72, and 5.39 times greater than those determined at similar stages in the enzymotic hydrolysis of the gamma benzylfructoside mixture. Invertase therefore hydrolyzed a constituent in the latter approximately 5.1 times more slowly than sucrose.

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Summary

1. Crystalline α-methylfructofuranoside, m. p. 80.5–81° and $[\alpha]^{20}D$ +93.0° in water, gave a new crystalline tetraacetate, m. p. 48–48.5° and $[\alpha]^{20}D$ +88.1° in chloroform, which was also prepared directly from sucrose.

2. An unstable, amorphous α-methyl glycoside–hydrogen chloride addition compound was precipitated when the constituents were mixed in anhydrous dioxane. The course of the subsequent decomposition was followed in more dilute solution both polarimetrically and by means of the copper reducing power. The behavior of gamma-fructosides dissolved in acid alcohols was in consequence assumed to depend on the formation of reducing, chlorine-containing substances which underwent change prior to their re-condensation with the solvent.

3. α-Methylfructofuranoside, when dissolved in benzyl alcoholic hydrogen chloride, was replaced very rapidly by a mixture of benzyl gamma-fructosides. Pure α-benzylfructofuranoside, m. p. 89°, $[\alpha]^{20}D$ +45.7° in water, was isolated from this mixture in the form of its crystalline tetraacetate, m. p. 84.5–85°, $[\alpha]^{20}D$ +64.7° in chloroform. Aqueous acid hydrolyzed the unsubstituted α-benzyl glycoside 16.5 times more rapidly than sucrose but it was unaffected by invertase.

4. Benzyl alcoholic hydrogen chloride partially converted α-benzylfructofuranoside into another non-reducing benzyl derivative of gamma-fructose which was not isolated. This benzyl derivative was hydrolyzed by invertase 5.1 times more slowly than sucrose. It had a specific levorotation of $[\alpha]^{20}D$ −27 ± 2° in water, calculated on the assumption that it possessed the molecular weight of a true benzylfructoside.

5. The constitutions of the crystalline α-methyl- and α-benzylglycosides described above were established by the methylation method. Tetramethyl α-benzyl- and α-methylfructofuranosides were liquids with refractive indices of $n^{19}D$ 1.4900 and $n^{20}D$ 1.4417, respectively, and with specific dextrorotations in chloroform of $[\alpha]^{19}D$ +83.3° and $[\alpha]^{20}D$ +115.9°, respectively. Both gave tetramethyl fructofuranose when hydrolyzed with aqueous acid.

6. Fear and Menzies' method of methylation with thallous ethylate and methyl iodide gave satisfactory results in the preparations described in (5).

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UNIVERSAL OIL PRODUCTS COMPANY]

The Cleavage of Side Chains in Aromatic Hydrocarbons in the Form of Paraffins by Means of Aluminum Chloride[1]

BY V. N. IPATIEFF AND HERMAN PINES

In the course of the study of polymerization of olefins,[2] alkylation[3] and depolyalkylation[4] of aromatic hydrocarbons, one of the chief difficulties in the identification of the reaction products was the lack of an adequate method for determining the structure of the alkyl group attached to the aromatic ring. It was tried[5] by a destructive hydrogenation method to convert the alkyl group to the corresponding paraffinic hydrocarbon. It was possible by this method to obtain methane and benzene from toluene; ethane and benzene from mono- and polyethylbenzene. However, in the case of propyl and butylbenzenes, the alkyl group was decomposed yielding methane, ethane and some propane. The

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(2) Ipatieff and Pines, *J. Ind. Eng. Chem.*, **27**, 1364 (1935); **28**, 684 (1936).

(3) (a) Ipatieff, Pines and Komarewsky, *ibid.*, **28**, 222 (1936); (b) Ipatieff, Corson and Pines, THIS JOURNAL, **58**, 919 (1936); (c) Ipatieff, Komarewsky and Pines, *ibid.*, **58**, 918 (1936).

(4) Ipatieff and Pines, *ibid.*, **58**, 1056 (1936).

(5) Ipatieff and Pines, in publication.