dene)-5-methoxyhydrindone-1.—A solution of 1.00 g. of the di-substituted hydroxylamine in 200 cc. of 2% aqueous potassium hydroxide was allowed to reflux for forty-eight hours. The insoluble material was separated and crystallized from alcohol; yield 23 mg.; m. p. 185–186.4°. The mixed m. p. with authentic 2-(5-methoxy-1-hydrindylidene)-5-methoxyhydrindone (m. p. 185.5–186.5°) described below showed no depression.

Anal. Calcd. for $C_{20}H_{18}O_3$: C, 78.41; H, 5.92. Found: C, 78.22; H, 6.13.

The dibasic acid was isolated from the alkaline solution according to the usual procedure[17]; crude yield 0.432 g. (36%[14]); m. p. 184–192° with previous softening. Crystallization from water gave material melting at 200–202°.

(*b*) *Under Mild Conditions. Isolation of 2-Cyano-5-methoxyhydrindone-1 and of 5-Methoxyhydrindone-1.*—A solution of 2.00 g. of the di-substituted hydroxylamine in 300 cc. of water containing 2.0 g. of potassium hydroxide and 6 cc. of alcohol was boiled for forty-five minutes by the end of which time the deep-purple color had changed to red. The cooled solution was washed with ether, acidified, and extracted with ether. The ether solution was washed thoroughly with 1% sodium bicarbonate solution, and then extracted with 5% potassium hydroxide solution which removed the cyano ketone. Acidification gave a brown suspension which was extracted with ether, dried, and purified by sublimation at 130–170° (0.1–0.5 mm.). Trituration of the sublimate with ether gave 0.065 g. of 2-cyano-5-methoxyhydrindone, m. p. 87–89°. Recrystallization from alcohol gave an almost colorless product, m. p. 94.5–95.5°, not depressed on admixture with authentic material, m. p. 96–96.5°.[6]

In another experiment 0.50 g. of di-substituted hydroxylamine was hydrolyzed for forty-five minutes with 160 cc. of 3% potassium hydroxide solution. The solution was cooled, filtered and extracted with ether. Evaporation of the dried (over anhydrous sodium sulfate) ether solution gave 0.10 g. (47% yield) of 5-methoxyhydrindone, m. p. 102–104°. After sublimation the m. p. was 108–109° and was not depressed on admixture with an authentic specimen.[6]

2-(5-Methoxy-1-hydrindylidene)-5-methoxyhydrindone-1. (*a*) *From 5-Methoxyhydrindone-1.*—5-Methoxyhydrindone-1[6] (1.0 g.) was boiled under reflux with 450 cc. of 10% potassium hydroxide solution for twenty-four hours. The golden suspension was separated and crystallized from methanol; yield 0.340 g. (36%); golden crystals, m. p. 185.5–186.5°. Further recrystallization did not change the melting point.

Anal. Calcd. for $C_{20}H_{18}O_3$: C, 78.41; H, 5.92. Found: C, 78.35, 78.44; H, 6.12, 6.14.

(*b*) *From 2-Hydroxymethylene-5-methoxyhydrindone-1.*—A solution of 0.199 g. of the hydroxymethylene ketone[6] in 70 cc. of 2% aqueous sodium hydroxide was treated according to the preceding procedure. The yield of recrystallized product was 0.024 g. (15%), m. p. 185.5–186.5°.

Hydrolysis of 2-hydroxymethylene-5-methoxyhydrindone-1[6] (282 mg.) in 7 cc. of 2% sodium hydroxide solution was carried out by refluxing for two hours. 5-Methoxyhydrindone-1 was obtained from the cooled mixture; yield 224 mg. (93%); m. p. 105–107°. Recrystallization from alcohol gave colorless needles, m. p. 109–110°, not depressed on admixture with an authentic specimen of the same m. p.[6]

Summary

The alkaline hydrolysis of some 2-cyanocyclohexanone derivatives and of some bis-(1-keto-2-cyclopentylidenemethyl)-hydroxylamine derivatives has been studied. Both of these types, which are readily available from the six- and five-membered ring ketones, respectively, are cleaved to dibasic acids. The over-all effect, therefore, is the opening of the ring of a cyclic ketone to produce a dibasic acid having one more carbon atom.

The mechanism of, and the effect of hydroxylamine on, the alkaline cleavage of the di-substituted hydroxylamines have been studied.

MADISON 6, WISCONSIN RECEIVED JULY 25, 1945

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY]

The Catalytic Glycosylation of Benzene with Sugar Acetates

BY CHARLES D. HURD AND WILLIAM A. BONNER[1]

The reaction between aromatic hydrocarbons and tetraacetylglucosyl chloride in the presence of large quantities of anhydrous aluminum chloride was described in an earlier communication.[2] From this reaction were isolated two unique carbohydrate products, each representing an entirely new class of carbohydrate derivative. Either product could be made predominant by varying the quantity of catalyst employed. Thus 1,1-diphenyl-1-desoxyglucitol pentaacetate was obtained as the sole product when the theoretical eight equivalents of catalyst were utilized, whereas tetraacetylglucopyranosylbenzene in the presence of about 20% of the diphenyl derivative could be isolated when only five equivalents of catalyst were present.

Previous studies have indicated that aluminum chloride, either alone[3] or in the presence of phosphorus pentachloride,[4] chlorinates the acylal function[5] of fully acetylated aldoses to yield the acetylated glycosyl chlorides. In view of this, it seemed likely that the glycosylation reaction might be accomplished by starting with the fully acetylated sugar rather than the chloride. Such a scheme assumes that the glycose acetate would undergo chlorination first at the acylal function, and that the intermediate chloride would then react with the aromatic hydrocarbon in the usual way, as illustrated below.

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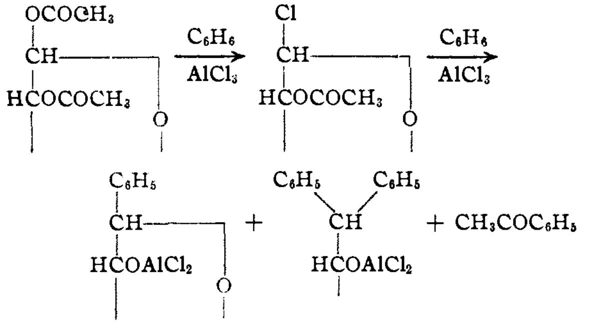
[1] Corn Products Refining Company Fellow, 1941–1944.

[2] Hurd and Bonner, THIS JOURNAL, **67**, 1664 (1945).

[3] Kunz and Hudson, *ibid.*, **48**, 1978, 2435 (1926); Hudson, *ibid.*, **48**, 2002 (1926).

[4] Von Arlt, *Monatsh.*, **22**, 144 (1901); Skraup and Kremann, *ibid.*, **22**, 375 (1901); Hudson and Johnson, THIS JOURNAL, **38**, 1223 (1916); Brauns, *ibid.*, **44**, 401 (1922); Richtmyer and Hudson, *ibid.*, **57**, 1716 (1935).

[5] Hurd and Cantor, *ibid.*, **60**, 2678 (1938); Hurd and Green, *ibid.*, **63**, 2201 (1941).



As a preliminary experiment, β-D-glucose pentaacetate was refluxed with aluminum chloride in chloroform to give a fair yield of tetraacetyl-α-D-glucosyl chloride. In addition, a considerable quantity of uncrystallizable sirup was obtained, having a specific rotation of 100° in chloroform. Whether or not this sirup represented an inversion product of the altrose type reported by Kunz and Hudson[3] was not determined.

The glucosylation of benzene was next undertaken. When benzene, β-D-glucose pentaacetate, and slightly over six equivalents of aluminum chloride were refluxed for several hours, a vigorous reaction ensued. The physical appearances attending the reaction exactly paralleled those described[2] for the analogous reaction employing tetraacetyl-α-D-glucosyl chloride. The reaction mixture was finally decomposed with water. From the benzene layer was isolated the anticipated acetophenone plus tar while the water layer yielded, after separation and acetylation, the same tetraacetyl-D-glucopyranosylbenzene and 1,1-di-phenyl-1-desoxy-D-glucitol pentaacetate which were previously obtained. The present reaction, however, gave a lower yield of product and much more tar.

Despite the inferior yield above, the greater availability of glucose pentaacetate over tetraacetylglucosyl chloride was a definite advantage, hence experiments were conducted to determine the optimum conditions for utilization of the former. In this study a series of reactions employing a fixed quantity of glucose pentaacetate was conducted under rigorously standardized conditions, the quantity of catalyst employed being the only variable. The yields of the various products plus certain significant ratios are summarized in Table I. Forty grams (0.1026 mole) of β-D-glucose pentaacetate was used in each experiment.

Referring to Table I, one sees that the rather wide variation in the ratio of crude carbohydrate to crude acetate is indicative of the diverse nature of the crude product throughout the five experiments. This is further emphasized by the widely fluctuating ratio of the amount of crystalline 1,1-diphenyl-1-desoxyglucitol pentaacetate to that of the purified acetate which could not be induced to crystallize. The investigation of these noncrystalline acetate residues has not been completed. Strangely enough, none of these five runs gave rise to isolable quantities of tetraacetylglucopyranosylbenzene despite the fact that the original smaller run, with conditions resembling experiment 3, gave a significant quantity of this compound. Regardless of this, the data in Table I indicate that the theoretical amount of aluminum chloride leads to the maximum yield of carbohydrate product.

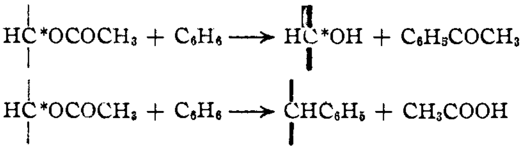
TABLE I

GLUCOSYLATION OF BENZENE USING VARYING QUANTITIES OF CATALYST

Run number	1	2	3	4	5
Aluminum chloride, g.	45.6	68.5	91.0	139.0	182.6
Aluminum chloride, moles	0.341	0.513	0.682	1.040	1.350
Aluminum chloride, % of theory[a]	33.0	50.0	66.5	101.5	133.3
Crude, unacetylated carbohydrate, g.	6.86	8.88	9.69	13.56	19.67
Crude acetate, g.	7.52	10.83	12.58	18.01	25.22
Crude carbohydrate/crude acetate	0.912	0.820	0.770	0.753	0.780
Purified acetate, g.	3.38	6.62	7.26	14.40	13.13
1,1-Diphenyl-1-desoxy-D-glucitol acetate, g.	0.00	0.00	1.75	9.41	6.15
Acetophenone, g.	0.00	10.9	18.4	28.0	35.9
Tar, g.	20.3	22.1	26.7	21.4	19.4

[a] By the theoretical quantity of aluminum chloride is meant ten moles for every mole of glucose pentaacetate.

The effect of the mole ratio of catalyst on the production of acetophenone and tar, as shown in Table I, is probably explainable in terms of the type of reaction favored at the acetyl groupings. It has been pointed out[6] that esters may react with aromatic hydrocarbons under the influence of aluminum chloride in two ways, giving acylation, alkylation, or both, depending on conditions. Thus in the presence of aluminum chloride the acetyl groupings of glucose pentaacetate might react according to one or both of the following equations.



$$\text{HC*OCOCH}_3 + \text{C}_6\text{H}_6 \longrightarrow \text{HC*OH} + \text{C}_6\text{H}_5\text{COCH}_3$$

$$\text{HC*OCOCH}_3 + \text{C}_6\text{H}_6 \longrightarrow \text{CHC}_6\text{H}_5 + \text{CH}_3\text{COOH}$$

The first of these equations, one of acylation, explains the formation of acetophenone and a stereochemically intact carbohydrate residue. The second equation, involving alkylation, would lead to mixtures of high molecular weight hydrocarbons of varying composition. Furthermore, since this reaction would rupture a bond at an asymmetric center, inversion or even racemization would be expected. The varying optical activity of the tars obtained in a second series of experiments, as well as their ready oxidation to large quantities of benzoic acid, support the assumption that the tars are formed as suggested by the second equation. Since both the ratio of

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(6) C. A. Thomas, "Anhydrous Aluminum Chloride," Reinhold Publishing Corp., 1941, pp. 673 ff.

catalyst and the reaction conditions influence the relative amount of alkylative and acylative cleavage in the reaction of ordinary esters with aromatic hydrocarbon,[6] it is not strange that these effects are here indicated in the varying amounts of acetophenone and tar produced. As seen in Table I, higher mole ratios of catalyst favor the production of acetophenone. Whereas most of this ketone is probably formed according to the first equation some may arise by way of the acetic acid of the second equation, especially if an excess of aluminum chloride is used.

It is apparent that the tars obtained in the earlier reported work[2] with tetraacetylglucosyl chloride must have been produced by the same mechanism. These tars were similar in appearance and their wide boiling range indicates their non-homogeneity.

The first extension of the catalytic glycosylation reaction to hexoses other than glucose was with β-D-galactose pentaacetate. In hopes of obtaining both D-galactosylbenzene and 1,1-diphenyl-1-desoxy-D-galactitol, only two-thirds of the theoretical quantity of catalyst was used. From the benzene layers acetophenone was obtained along with a considerable quantity of tar which had a vile, penetrating odor. The water layers, after acetylation, yielded levorotatory, uncrystallizable sirups. Deacetylation of the latter gave a sirup separable into two products by crystallization from water. The more insoluble product was a dextrorotatory, white powder which was shown by analysis and by oxidation to benzophenone to be 1,1-diphenyl-1-desoxy-D-galactitol; acetylation of it gave rise to the corresponding pentaacetate, a levorotatory, glassy substance. The more soluble product was a sirup containing D-galactopyranosylbenzene. Its acetate, $[\alpha]_D$ 0.54°, also was sirupy, and oxidation of it with permanganate led to the isolation of both benzophenone and benzoic acid, in amounts pointing to a mixture containing 91% tetraacetylgalactopyranosylbenzene and 9% 1,1-diphenyl-1-desoxygalactitol pentaacetate. Hence, the galactosylation reaction was quite analogous to the previous glucosylation. These data permit a rough calculation of the specific rotation of pure tetraacetyl-D-galactopyranosylbenzene by extrapolating the straight line connecting the values for pure 1,1-diphenyl-1-desoxygalactitol pentaacetate (−98.4°) and for the mixture (0.54°) of 9% of this and 91% of tetraacetylgalactopyranosylbenzene. Extrapolation gives a value of about 9° for the specific rotation of pure tetraacetyl-D-galactopyranosylbenzene.

The above argument rests on several experimentally verified assumptions. First, the assumption of equal oxidation yields for each component in the acetate mixture ($[\alpha]_D$ 0.54°) was verified by the oxidation of a mixture of comparable composition of the corresponding glucose derivatives, and the isolation of comparable quantities of benzophenone and benzoic acid. Secondly, the assumption of a linear relation between the specific rotation and composition of mixtures, permitting determination of an unknown specific rotation by extrapolation, was verified on several binary carbohydrate mixtures of known composition, namely, the two corresponding glucose derivatives, α- and β-D-glucose pentaacetate, and phenyl tetraacetyl-α- and -β-D-glucosides. The third assumption, that the acetate mixture which was oxidized contained only the two components, is of course not readily verifiable; but it is felt that the quantity of any other component present would be sufficiently low not to alter the conclusion greatly.

In an extension of the glycosylation reaction to the pentose series, the reaction of benzene with β-D-xylose tetraacetate gave results similar to those already noted. Tar formation, however, was so excessive that no acetophenone was obtained. From the water layer was obtained triacetyl-D-xylopyranosylbenzene. By the deacetylation of the sirup resulting on evaporation of the mother liquors from the crystallization of the above compound, there was obtained crystalline 1,1-diphenyl-1-desoxy-D-xylitol. Each compound consisted of fine, white needles. Oxidation of the former yielded benzoic acid, and the latter benzophenone.

A pyranose ring structure is indicated in naming each of the above monophenyl derivatives. The logic behind the assumption of the retention of the parent ring size has been presented earlier[2] for glycosylations employing tetraacetylglucosyl chloride, and similar considerations apply in the present instances. Actual proof of this point will be considered in a later communication.

Preliminary attempts have been made to apply the glycosylation reaction to 2,3,4,6-tetramethyl-D-glucose as a typical member of another series of sugar derivatives, the methyl ethers. Similarly, exploratory investigations of other typical alkylation catalysts such as boron fluoride and hydrogen fluoride have been undertaken. In these cases, however, the studies are as yet incomplete, and no generalizations are possible.

Experimental

Benzene and Glucose Pentaacetate

β-D-Glucose pentaacetate (20 g.), benzene (300 ml.), and 95% aluminum chloride (45 g.) were placed in the usual apparatus[2] and refluxed for five to six hours. The reaction mixture was cooled, decomposed with water, and worked up as previously described. From the benzene layers were obtained 11.4 g. of acetophenone (b. p. 195–212°) and 9.6 g. of residual tar. The identity of the ketone was established as before through the 2,4-dinitrophenylhydrazone, m. p. 249° (uncor.). The crude acetylation product from the water layer and pyridine extraction was an amber sirup weighing 4.4 g. This was crystallized from 2-propanol to give a white solid, m. p. 97–143°, which was recrystallized from the same solvent. On collection of the crystals two distinct types were discernible, and could be separated manually: (1) small needles (0.3 g.) of tetraacetylglucopyranosylbenzene, m. p. 149.5–151.5°, and (2) large cubes (0.4 g.) of 1,1-diphenyl-1-desoxy-D-glucitol pentaacetate, m. p. 94–96°. Neither product showed melting point depressions with authentic samples.

A Study of Yields as a Function of Quantity of Catalyst

β-D-Glucose pentaacetate (40 g.), benzene (600 ml.) (dried by distillation), and anhydrous aluminum chloride containing 7% alumina (by sublimation analysis) were used. Weights of aluminum chloride taken in the several experiments are recorded in Table I.

The usual apparatus was employed. Refluxing times were five hours, except in run 1 which was six hours, since the catalyst phase would not dissolve and stirring had to be discontinued. At the end of the reaction the mixture was cooled, left to stand overnight, and was then poured slowly into water (1800 ml.). The two phases were stirred vigorously for half an hour, then were separated. The benzene layer was washed with two 250-ml. portions of water, and the water phase with two 200-ml. portions of benzene, the washes being combined with their appropriate phases.

Benzene Layer.—In each case this was dried over sodium sulfate, filtered, and the solvent removed on the steam-bath (vacuum for several minutes at the end). The residue was transferred to a weighed 125-ml. distilling flask and distilled at atmospheric pressure into three fractions: (1) benzene; (2) acetophenone, collected from 190–215°, except in run 1 where decomposition started about 150°; (3) tarry material, boiling above 215°.

Water Layer—In each run the water layer was neutralized to litmus with 20% sodium hydroxide, and the alumina filtered with the aid of Celite. The alumina cake was washed twice by suspending evenly in water (1000 ml.) boiling, and filtering hot. The filtrate and washings were reduced to dryness by distillation (steam-bath) *in vacuo* from a one-liter, three-necked flask. The residue was scraped out and powdered. This was then extracted with two 200-ml. and two 150-ml. portions of boiling pyridine, filtering the solution after each extraction. The pyridine solution was distilled to dryness *in vacuo* at 100° from a weighed 125-ml. flask, the last traces of pyridine being removed by vacuum distilling toluene (25 ml.) from the residues. The weighed residue corresponds to "Crude, unacetylated carbohydrate" in Table I.

Acetylation.—The crude sirup from above was dissolved in pyridine (10 ml. per gram of sirup) at 100°, cooled, treated with acetic anhydride (5 ml. per gram), and the mixture permitted to stand for two days. The volatile constituents were then vacuum distilled at 100°. The residue was heated at 100° (8 mm.) for ten minutes, toluene added, and vacuum distilled, and the residue heated an additional ten minutes at 100° (8 mm.). The weighed residue corresponds to "crude acetate" in Table I.

Purification of Acetate.—The crude acetate was dissolved in warm acetone (2 ml. per g. of acetate), and poured into a system containing 75% ether and 25% water (10 ml. ether per gram of acetate). The two phases were separated and the ether phase washed twice with water (5 ml. per g.), twice with 4 *N* hydrochloric acid (2.5 ml. per g.), twice with water (5 ml. per g.), twice with saturated sodium bicarbonate solution (2.5 ml. per g.), and finally with water (5 ml. per g.). The washed ether solution, kept up to its original volume by addition of solvent after each washing, was dried over sodium sulfate for eighteen hours, then decolorized by filtration through a bed of a spatulaful of Celite under four spatulafulls of Norit. The solvent was then removed on the steam-bath, with reduced pressure at the end. The weight of the residual syrup corresponds to "purified acetate" in Table I.

Crystallization.—Each sample of pure acetate was taken up in 2-propanol (2 ml. per g. of purified acetate), stoppered, and permitted to crystallize for several days. All of the crystalline material isolated was pure 1,1-diphenyl-1-desoxy-D-glucitol pentaacetate. Melting point and mixed melting point determinations were all 94–95°.

A Study of Yields as a Function of Time

A series of small experiments comparable to the previous set was run, in which the optimum quantity of catalyst was employed, and time was the variable. In each run β-D-glucose pentaacetate (10 g., 0.0255 mole), benzene (150 ml.), and aluminum chloride (34 g., 0.255 mole) were placed in the usual apparatus and stirred under reflux for the specified length of time. The mixture was then cooled and cautiously decomposed with cold water (100 ml.). Emulsions formed in some cases (notably Runs 5 and 6, Table II) and were broken by filtration through Celite. The layers were separated, and the benzene layer washed twice with 100-ml. portions of hot water (50°).

Benzene Layer.—After drying over sodium sulfate the solvent was removed and the residue fractionated at aspirator pressures into acetophenone (A) (b. p. 155–170°) and tar (B). The distillation was stopped when the temperature began to fall after collection of the acetophenone fraction. (The letters A, B and others to follow refer to headings in Table II).

Tars.—The residual tar was dissolved in ether (10 ml. per g. of tar) and filtered through Norit (2 g. per g. of tar). The solvent was removed and the rotation (D) of the partially decolorized sample (C) taken in chloroform (E, grams of C per 100 ml. of chloroform). One-half gram of each tar sample was oxidized by refluxing four hours with potassium permanganate (3.0 g.) in saturated sodium hydroxide solution (1.5 ml.) and water (50 ml.). Concentrated sulfuric acid (3 ml.) was cautiously added, then enough bisulfite to discharge the permanganate color, the mixture boiled, and filtered hot. The manganese dioxide residue was washed thoroughly with hot water and acetone, and the filtrate and washings extracted twice with 20 ml. of ether. The extract was washed twice with 10% sodium hydroxide solution to remove organic acids, then with water, and finally dried over sodium sulfate, filtered, and the solvent removed. The residue (F) was a thick, aromatic smelling sirup. The aqueous layer was acidified and extracted with ether, the extract washed with water, dried, and the solvent removed, leaving benzoic acid (G), m. p. after recrystallization 119.5–120.5°. The total sirupy neutral residues (F) from the six runs (0.65 g.) was combined and reoxidized with alkaline permanganate. As a result, 0.10 g. more of benzoic acid was formed and 0.24 g. of neutral material which failed to give a 2,4-dinitrophenylhydrazone.

Water Layer.—The water layers from the original reactions were heated to 50° and extracted with 60 ml. of benzene, which was combined with the original benzene layer before its work-up. The water layer was then neutralized in the hot with 40% sodium hydroxide solution, boiled, and the aluminum hydroxide filtered with suction while hot. The cake was washed with 100 ml. of boiling water. The filtrate was reduced to dryness *in vacuo*, and the residue acetylated by stirring with acetic anhydride (70 ml.) and sodium acetate (3 g.) for three hours on the steam-bath. The mixture was cooled, poured into water, and allowed to stand overnight. The solution was extracted twice with 50-ml. portions of ether, and the extract washed with water, saturated sodium bicarbonate, again with water, then dried and decolorized by filtration through a small bed of Norit. Removal of the solvent left a clear sirupy acetate (H) which was deacetylated in each case by dissolving in methanol (10 ml.), and adding a small chip of sodium. The solid (J) was filtered off after two hours. After recrystallization from water the 1,1-diphenyl-1-desoxy-D-glucitol hydrate melted at 156.5–157.5°, $[\alpha]^{25}\text{D}$ 47.4° (*c*, 1.680; dioxane).

Table II gives the pertinent data relating to these experiments.

Benzene and β-D-Galactose Pentaacetate

β-D-Galactopyranose pentaacetate (20 g.) (prepared by the procedure of Erwig and Königs[7]), benzene (300 ml.), and aluminum chloride (45 g.) were heated for five hours on the steam-bath under customary conditions. The product was worked up as before. From the benzene layer was obtained 23.1 g. of an oil, which fractionated into benzene, 8.7 g. of acetophenone, and 11.3 g. of tar. The ke-

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[7] Erwig and Königs, *Ber.*, **22**, 2207 (1889).

TABLE II

GLUCOSYLATION OF BENZENE UNDER VARYING REACTION TIMES

Run	Time, hr.	A, g.	B, g.	C, g.	D, $[\alpha]^{25}\text{D}$	E g.	F, g.	G, g.	H, g.	J, g.
1	4	2.88	5.47	2.66	1.73	1.155	0.09	0.07	1.48	0.62
2	8.5	1.03	6.11	3.40	15.10	2.654	.10	.09	1.17	.42
3	15	3.62	4.63	2.76	−2.85	2.105	.11	.10	1.45	.60
4	24	4.30	5.93	3.71	2.62	4.207	.07	.15	1.80	.76
5	48	5.01	5.75	3.06	−2.18	2.756	.17	.10	1.25	.44
6[a]	8	5.76	3.06	1.60	8.84	1.700	.11	.11	0.70	.32

[a] Tetraacetyl-α-D-glucosyl chloride (9.4 g., 0.2554 mole) was used instead of glucose pentaacetate. Everything else was identical.

tone was identified through the semicarbazone, m. p. 199.5–200.5°, which showed no melting point depression with an authentic sample. The pyridine extraction residue from the water layer weighed 6.15 g., and was acetylated in the usual way to give 4.04 g. of a clear amber glass having a specific rotation of −24.6°, in chloroform. A duplicate experiment yielded 3.70 g. of a clear syrup having a specific rotation of −37.3°. Neither sirupy acetate could be crystallized.

Deacetylation.—The above 3.70 g. of sirup was taken up in methanol (125 ml.) and deacetylated in the usual way with a chip of sodium. Removal of solvent left 2.17 g. of an amber sirup whose solution in water yielded crystals after standing several hours. The mother liquor (L) is mentioned below. After three days the crystals were collected. They weighed 1.75 g. Part of the solid was removed for oxidation and the remainder recrystallized twice from water to give 1,1-diphenyl-1-desoxy-D-galactitol, m. p. 174°; $[\alpha]^{27}\text{D}$, 28.6° (*c*, 0.455; acetone). As obtained, this material was a white powder which was definitely crystalline when examined under a lens.

Anal. (by T. S. Ma) Calcd. for $C_{18}H_{22}O_5$: C, 68.0; H, 6.92. Found: C, 67.70; H, 7.35.

One-half gram of the crude substance was oxidized with alkaline permanganate, to yield 0.1 g. of benzophenone, identified through the 2,4-dinitrophenylhydrazone, m. p. 241–242° (uncor.).

Acetylation of 1,1-Diphenyl-1-desoxygalactitol.—A sample of 1,1-diphenyl-1-desoxy-D-galactitol (0.35 g.), m. p 172.5–173°, was dissolved in pyridine (8 ml.). Then acetic anhydride (5 ml.) was added. After standing for five days the mixture was poured into water, allowed to stand several hours, extracted into ether, and the product purified by washing with water, 4 *N* hydrochloric acid, water, sodium bicarbonate solution, and water, then isolated as usual. The 1,1-diphenyl-1-desoxy-D-galactitol pentaacetate was a clear glass weighing 0.58 g. (99.5%), and had a specific rotation, $[\alpha]^{25}\text{D}$, of −98.4° in chloroform (*c*, 3.430). The glass failed to crystallize from 2-propanol, so the solvent was removed and the residue dried for an extended period *in vacuo* over phosphoric anhydride.

Anal. (by T. S. Ma) Calcd. for $C_{28}H_{32}O_{10}$: C, 63.6; H, 6.06. Found: C, 63.29; H, 6.12.

Treatment of Mother Liquor from Deacetylation.—The aqueous mother liquors (L) obtained on deacetylation and crystallization of the crude galactosylation product were evaporated to dryness to give 0.97 g. of an amber sirup. This was reacetylated in the usual way using pyridine (15 ml.) and acetic anhydride (15 ml.) to give 1.24 g. of a clear, amber sirupy acetate having a specific rotation of 0.54° in chloroform. One-half gram of this sirup was removed and oxidized with alkaline permanganate to give 0.1 g. of a white solid. This was dissolved in a small volume of dilute sodium hydroxide solution and extracted with ether. Evaporation of the ether yielded 0.01 g. of benzophenone, identified through the 2,4-dinitrophenylhydrazone. Acidification of the aqueous layer, followed by ether extraction, washing, drying, and solvent-evaporation yielded 0.09 g. of slightly impure benzoic acid, m. p. 118.5–120.5°, after one recrystallization.

Oxidation of Known Mixtures.—A mixture containing 10% (0.05 g.) of 1,1-diphenyl-1-desoxy-D-glucitol pentaacetate and 90% (0.45 g.) of tetraacetyl-D-glucopyranosylbenzene was oxidized and worked up as in the previous experiment. From the ether layer was obtained 0.01 g. of benzophenone, and from the aqueous layer 0.06 g. of benzoic acid. From these data the percentage composition of the mixture oxidized is calculated to be 12.4% of 1,1-diphenyl-1-desoxyglucitol pentaacetate and 87.6% of tetraacetylglucopyranosylbenzene, as against the known composition of 10 and 90%, respectively.

Benzene and β-D-Xylose Tetraacetate

β-D-Xylose tetraacetate (20 g.), benzene (300 ml.), and aluminum chloride (30 g.) were heated under reflux for two and a half hours, then worked up as before. Removal of solvent from the benzene layer left 20.8 g. of very viscous brown oil. The product from a previous run decomposed when distilled at atmospheric pressures. When the 20.8 g. was distilled at 2 mm. only a trace (0.1 g.) of acetophenone (bath temp. 125°) was obtained, along with 3.3 g. of an amber glass (bath temp. 180°), and 17.4 g. of a residual black tar. The acetophenone was identified only by its odor, and the higher fractions were not investigated.

The separation and acetylation of the product in the water layer led to 0.82 g. of a light, amber sirupy acetate. This was crystallized from 2-propanol to give 0.17 g. of white needles, m. p. 166–167°. One recrystallization brought the m. p. to 169.5°, unchanged by a second recrystallization. The specific rotation in chloroform, $[\alpha]^{25}\text{D}$ was −57.7° (*c*, 0.390). A sample of the acetate was oxidized in the usual fashion to yield benzoic acid, confirming the structure as triacetyl-D-xylopyranosylbenzene.

Anal. (by T. S. Ma). Calcd. for $C_{17}H_{20}O_7$: C, 60.8; H, 6.00. Found: C, 60.40, H, 6.02.

The solvent was removed from the mother liquors of the above crystallization of the original sirupy acetate mixture, and the residue, 0.65 g. of a sirup, was deacetylated in the usual manner in methanol (25 ml.). After removal of the solvent *in vacuo* there was left 0.43 g. of a yellow sirup. This was dissolved in hot water, concentrated in an air stream until solidification began, redissolved, and clarified by filtration through Norit and Celite. Further concentration gave rise to about 0.10 g. of fine, white needles, m. p. 163–163.5°. Three-fourths of the crop was oxidized with alkaline permanganate to yield benzophenone, identified by the 2,4-dinitrophenylhydrazone, m. p. 239–240° (uncor.). The remainder of the crop was recrystallized from water to give a solid melting at 167–168°; $[\alpha]^{26}\text{D}$, 73.2° (*c*, 0.280; dioxane). Analysis confirmed this as 1,1-diphenyl-1-desoxy-D-xylitol.

Anal. (by T. S. Ma). Calcd. for $C_{17}H_{20}O_4$: C, 70.9; H, 7.00. Found: C, 70.70; H, 7.10.

Summary

The glycosylation of benzene with fully acetylated sugars has been shown to proceed in the presence of aluminum chloride. The products of the reaction are acetophenone, glycopyranosylbenzenes, and the corresponding 1,1-diphenyl-1-desoxyalditols. The reaction has been applied to glucose, galactose, and xylose. With glucose,

the yields are less than those obtained using tetraacetyl-α-D-glucosyl chloride as the alkylating agent. A study has been made of the optimum mole ratio of catalyst for the promotion of the reaction employing β-D-glucose pentaacetate, and it has been shown that the theoretical quantity of catalyst gives highest yields.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Bromination of Phenyl Tetraacylglucosides

BY CHARLES D. HURD AND WILLIAM A. BONNER[1]

In a series of experiments dealing with the chemical similarities between phenyl glycosides and phenyl ethers, we have found that phenyl tetraacylglucosides may be brominated directly to give excellent yields of a monobromination product. The entering substituent has been shown to occupy the *para* position by hydrolysis to *p*-bromophenol and by direct synthesis of *p*-bromophenyl tetraacetyl-β-D-glucopyranoside by the Helferich and Schmitz–Hillebrecht fusion procedure.[2]

Experimental

***p*-Bromophenol Tetraacyl-D-glucosides by Bromination.**—One gram of phenyl tetraacetyl-β-D-glucopyranoside was dissolved in 20 ml. of acetic acid, and 1.5 ml. of bromine was added. The mixture was permitted to stand for one hour, then poured into water (100 ml.). The milky, red suspension was extracted with ether (100 ml.), and the extract washed twice with water, with 10% sodium hydroxide solution (until the bromine color was removed), and again twice with water. After drying over anhydrous sodium sulfate the solvent was removed to give 1.05 g. of crude *p*-bromophenyl tetraacetyl-β-D-glucopyranoside. This was recrystallized twice from 2-propanol to give a pure product, m. p. 133°, $[\alpha]^{25}D$ −17.8° (*c*, 1.320; $CHCl_3$). The analyses below were performed by Dr. T. S. Ma.

Anal. Calcd. for $C_{20}H_{23}O_{10}Br$: C, 47.73; H, 4.61. Found: C, 48.30; H, 4.65.

Phenyl tetraacetyl-α-D-glucopyranoside (0.50 g.) was treated in the same manner, using proportional quantities of reagents. The crude reaction product (0.55 g.) was taken up in 2-propanol, filtered through Norit, and the filtrate permitted to crystallize for several days. Fine, white platelets of *p*-bromophenyl tetraacetyl-α-D-glucopyranoside resulted, m. p. 113°, $[\alpha]^{25}D$ 159.6° (*c*, 1.505; $CHCl_3$).

Anal. Calcd. for $C_{20}H_{23}O_{10}Br$: C, 47.73; H, 4.61. Found: C, 48.00; H, 4.51.

When phenyl tetrapropionyl-β-D-glucoside was treated analogously (in propionic acid as solvent), long, white needles of *p*-bromophenyl tetrapropionyl-β-D-glucopyranoside resulted, m. p. 78.5–79°, $[\alpha]^{25}D$ −13.7° (*c*, 1.530; $CHCl_3$).

Anal. Calcd. for $C_{24}H_{31}O_{10}Br$: C, 51.52; H, 5.60. Found: C, 51.34; H, 5.43.

Isolation of Phenolic Aglucone.—*p*-Bromophenyl tetraacetyl-β-D-glucoside (1.50 g.), prepared as above, was added to methanol (65 ml.) and a chip of sodium was added. After three hours the solvent was removed *in vacuo* to yield the deacetylated product. Attempts to crystallize this from water led to a gel. The product was therefore dissolved in water (35 ml.), concd. hydrochloric acid (15 ml.) added, and the mixture refluxed for one hour. After cooling and adding salt, the mixture was extracted with ether. The extract was washed, dried, decolorized, and the solvent removed to yield 0.48 g. (93%) of *p*-bromophenol. Its identity was established by benzoylation using benzoyl chloride (2 ml.) and pyridine (2 ml.), warming on the steam-bath and then pouring into water. The product was extracted into ether, and the extract washed with water, dilute hydrochloric acid, water, 5% sodium hydroxide, and again with water. On drying, decolorizing, and removing the solvent, *p*-bromophenyl benzoate was isolated, m. p. 101.5–102° after one recrystallization from benzene and petroleum ether. This ester showed no mixed m. p. depression (101–102°) with an authentic sample of *p*-bromophenyl benzoate (m. p. 101–102°).

Direct Synthesis of *p*-Bromophenyl Tetraacetyl-β-D-glucopyranoside.—β-D-Glucose pentaacetate (5.0 g.), *p*-bromophenol (11.4 g.), and a trace of *p*-toluenesulfonic acid were fused *in vacuo* for one hour at 100°. The melt was taken up in ethylene chloride and the solution was washed with water, 10% sodium hydroxide solution till the water layer extracted no colored material, again with water, and then dried over sodium sulfate. Removal of the solvent left 5.1 g. (79%) of crude glucoside. After two recrystallizations from 2-propanol the product had m. p. 131.5–132°, $[\alpha]^{25}D$ −17.0° (*c*, 6.565; $CHCl_3$), and showed no mixed m. p. depression (131.5–132°) with the corresponding glucoside prepared by direct bromination.

Summary

Phenyl tetraacetyl-β-D-glucopyranoside, its α isomer, and phenyl tetrapropionyl-β-D-glucoside have been converted by direct bromination into the corresponding *p*-bromophenyl tetraacetyl-D-glucosides. *p*-Bromophenyl tetraacetyl-β-D-glucoside was synthesized also from *p*-bromophenol and β-D-glucose pentaacetate.

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[1] Corn Products Refining Company Research Fellow, 1941–1944.

[2] Helferich and Schmitz-Hillebrecht, *Ber.*, **66**, 378 (1933); Montgomery, Richtmyer and Hudson, THIS JOURNAL, **64**, 690 (1942).