DEBENZYLATION OF CARBOHYDRATE BENZYL ETHERS AND BENZYL GLYCOSIDES VIA FREE-RADICAL BROMINATION*

JAMES N. BEMILLER AND HOWARD L. MUENCHOW

Department of Chemistry and Biochemistry, Southern Illinois University at Carbondale, Carbondale, Illinois 62901 (U. S. A.)

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ABSTRACT

The dealkylation of benzylated carbohydrates by free-radical bromination and hydrolysis has been further examined. Free-radical bromination of methyl 2,3,4,6tetra-O-benzyl- α -D-glucopyranoside (1), methyl 2,3-di-O-benzyl- α -D-glucopyranoside (2), 6-O-benzyl-3,5-O-benzylidene-1,2-O-isopropylidene- α -D-glucofuranose (4), and 6-O-benzyl-D-glucose (3) appears to be quantitative. Spectroscopic evidence of a C-Br bond indicates that an α -bromobenzyl ether is the product. Alkaline hydrolysis yielded methyl α -D-glucopyranoside from 1 and 2 and D-glucose from 3 and 4. A benzyl group present as an aglycon could be removed in the same way. Reaction of benzyl α -D-glucopyranoside tetraacetate (6) with bromine and chlorine under freeradical conditions and examination of the products by t.l.c. and i.r. spectrophotometry indicated that the first product was an α -halobenzyl glycoside and that the aglycon could be displaced by Br⁻ or Cl⁻ to form the tetra-O-acetyl-D-glucopyranosyl halide, undoubtedly with anomerization. Treatment of the mixture of products with moist ether and silver carbonate yielded only 2,3,4,6-tetra-O-acetyl-D-glucopyranose.

INTRODUCTION

BeMiller, Wing, and Meyers¹ described a new method of debenzylation of carbohydrate derivatives that involves free-radical bromination of one of the methylene hydrogen atoms of the benzyl ether to form a stable α -bromobenzyl ether in apparently quantitative yield. This compound was then subjected to mild alkaline hydrolysis to yield benzaldehyde and the carbohydrate, with complete retention of configuration.

Preferential abstraction of a benzylic hydrogen atom and rapid hydrolytic cleavage of the α -bromobenzyl ether were not unexpected, as both reactions are well documented²⁻⁹. What was surprising was the quantitative formation of the α -bromobenzyl ether, as it had been reported that alkyl benzyl ethers react rapidly with bromine to form benzaldehyde and an alkyl bromide directly through decomposition of either the radical R-O-CH-Ph^{2.3} or the α -bromobenzyl ether R-O-CHBr-Ph⁴⁻⁸.

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^{*}Dedicated to Dr. Louis Long, Jr., in honor of his 70th birthday.

Two possible explanations for the formation of the stable α -bromobenzyl ethers of carbohydrates have been presented¹⁰. One is that, energetically, cleavage into benzaldehyde and a carbohydrate radical is not favorable. Not only would such a radical be substantially less stable than the alkyl radical because of the plurality of electronegative oxygen atoms attached to vicinal carbon atoms, but also because of the increased magnitude of the non-bonded interactions and eclipsing arising from sp² (radical) rather than sp³ (ground state) geometry; the latter is extensive in pyranoid rings.

If the cleavage usually involves a four-centered transition state without prior dissociation into an alkyl radical or prior formation of an α -bromobenzyl ether, cleavage should proceed faster with increased nucleophilic character of the alkyl group as both the bromine and oxygen atoms are electrophilic, and stability would be gained by the formation of benzaldehyde and an alkyl bromide. Because a carbohydrate moiety is much less nucleophilic than an alkyl group, and because of steric inhibition to the approach of bromine, cleavage of carbohydrate ether radicals by this route would be unlikely.

Neither explains well the reaction at the primary position.

This investigation was undertaken to obtain additional evidence for the mechanism of the reaction and the apparent stability of the α -bromobenzyl ether derivatives; to determine if there are differences in reaction at C-1, C-2, C-3, C-4, and C-6 of the D-glucopyranose ring; to investigate the reaction of benzyl ether derivatives of D-glucose with other free-radical sources; and to gain evidence for further applicability of the method.

RESULTS AND DISCUSSION

When methyl 2,3,4,6-tetra-O-benzyl- α -D-glucopyranoside (1) was treated with di-*tert*-butyl peroxide in carbon tetrachloride, no reaction occurred. Addition of bromine to the reaction mixture immediately produced hydrogen bromide and a precipitate. Alkaline hydrolysis¹ yielded methyl α -D-glucopyranoside and incompletely debenzylated compounds.

Methyl 2,3-di-O-benzyl- α -D-glucopyranoside (2) in benzene solution protected from light had not reacted after 5 h at room temperature in the presence of excess bromine. Illumination of the solution produced hydrogen bromide and a precipitate that gave benzaldehyde (2,4-dinitrophenyl)hydrazone on treatment with aqueous (2,4-dinitrophenyl)hydrazine reagent, that gave methyl α -D-glucopyranoside upon alkaline hydrolysis, and that had an i.r. absorbance indicative of a carbon-bromine bond. Thus, it was concluded that the precipitate was the α -bromobenzyl ether.

Reaction of 2 with chlorine in chloroform under free-radical conditions also produced a gummy precipitate which, when exposed to room air, yielded crystalline methyl α -D-glucopyranoside.

Treatment of 2 with di-*tert*-butyl peroxide in chloroform for 2 weeks gave no reaction.

6-O-Benzyl-D-glucose (3) was treated with bromine under conditions similar to those used with 2. The syrupy precipitate that formed during the bromination reaction gave D-glucose and benzaldehyde when treated with aqueous reagents, indicating that it was the α -bromobenzyl ether.

6-O-Benzyl-3,5-O-benzylidene-1,2-O-isopropylidene- α -D-glucofuranose (4) in benzene solution, when treated with bromine under free-radical conditions, yielded a syrupy precipitate that gave D-glucose after alkaline hydrolysis. Hence, the bromination reaction also removed the benzylidene and isopropylidene groups, presumably through the production of HBr in the case of the isopropylidene group and, perhaps, by bromination in the case of the benzylidene group.

The initial step in the reaction of bromine with a carbohydrate benzyl ether is apparently the preferential free-radical abstraction of one of the methylene hydrogen atoms by a bromine atom¹. This reaction is effected by light, indicating that it is a free-radical reaction. Free radicals were not detected by e.p.r. spectrometry. Irradiation of the reaction system while in the e.p.r. sample-cavity was successful in producing a reaction between bromine and the various compounds as evidenced by production of hydrogen bromide. However, none of these reactions produced a recorded free-radical spectrum. A flow system designed to give positive irradiation of the sample before it entered the e.p.r. sample cavity, and variation of the flow rate of the reaction mixture through the system also failed to allow detection of free radicals, although reaction occurred during the recording of spectra. It is concluded that radical detection was not successful either because radicals were formed in low concentration, or because they have a short half-life on the e.p.r. time-scale, or both.

The radical so formed may react with a molecule of bromine to form an α -bromobenzyl derivative¹. When R was a D-glucose moiety containing benzyloxy groups at C-2, C-3, C-4, or C-6 in various combinations, the reaction was apparently quantitative. Methyl 2,3,4,6-tetra-O-benzyl- α -D-glucopyranoside (1), methyl 2,3-di-O-benzyl- α -D-glucopyranoside (2), 6-O-benzyl-3,5-O-benzylidene-1,2-O-isopropylidene- α -D-glucofuranose (4), and 6-O-benzyl-D-glucose (3) formed amorphous precipitates. Reaction of the precipitates, which have a C-Br bond as determined by i.r. spectrophotometry, with aqueous (2,4-dinitrophenyl)hydrazine reagent produced benzaldehyde (2,4-dinitrophenyl)hydrazone. Thus, it can be inferred that the insoluble compound formed by the reaction of bromine radicals with D-glucose derivatives that have benzyloxy groups at C-2, C-3, C-4 or C-6 in various combinations is the α -bromobenzyl ether. It also appears that formation of the α -bromobenzyl derivative is the terminating step of the reaction for D-glucose derivatives having benzyloxy groups at C-2, C-3, C-4, and C-6.

From the data presented here, it can be hypothesized that the mechanism for reaction of D-glucose derivatives having benzyloxy groups at C-2, C-3, C-4, and C-6 is as follows¹ (R = D-glucose moiety):

 $\begin{array}{rcl} & Br_2 & \longrightarrow & 2Br \cdot \\ R-O-CH_2-Ph + Br \cdot & \longrightarrow & R-O-\dot{C}H-Ph + HBr \\ R-O-\dot{C}H-Ph + Br_2 & \longrightarrow & R-O-CHBr-Ph + Br \cdot \end{array}$

Benzyl α,β -D-glucopyranoside (5) (benzyloxy group at C-1) also formed a precipitate, apparently the α -bromobenzyl glycoside, when treated with bromine under irradiation. Alkaline hydrolysis of the precipitate yielded D-glucose.

When this compound was fully acetylated, a precipitate did not form. Benzyl 2,3,4,6-tetra-O-acetyl- α -D-glucopyranoside (6) in benzene solution was treated with an excess of bromine under free-radical conditions. Removal of the solvent followed by reaction of the residue with moist ether and silver carbonate gave a product that corresponded to authentic 2,3,4,6-tetra-O-acetyl-D-glucopyranose by t.l.c. Thus, benzyl glycoside groups can be removed in the same way as benzyl ether groups.

Another solution of 6 in carbon tetrachloride was cooled to -30° before bromine was added. The solution was then carefully irradiated to keep the temperature at about -30° . Following reaction, 2 components were present, namely, starting material and the α -bromobenzyl glycoside.

A third solution of 6 in benzene was treated with chlorine under free-radical conditions. Following removal of the solvent and treatment of the residue with moist ether and silver carbonate, this reaction also gave 2,3,4,6-tetra-O-acetyl-D-gluco-pyranose.

Efforts to isolate the products formed during the reactions of $\mathbf{6}$ with bromine and chlorine were unsuccessful as the products decomposed.

Benzyl 2,3,4,6-tetra-O-acetyl- β -D-glucopyranoside (7) was treated with bromine and chlorine under conditions similar to those employed with the α -D anomer. The results were identical to those obtained with the α -D anomer.

Thus, benzyl 2,3,4,6-tetra-O-acetyl- α -D-glucopyranoside (6) forms only the α -bromobenzyl glycoside when brought into reaction with bromine radicals at -30° . At room temperature, 6 gives two compounds when treated with a slight excess of bromine in the presence of light. One of these compounds corresponds in R_F value to the compound believed to be the α -bromobenzyl glycoside. The other compound corresponds in R_F value to 2,3,4,6-tetra-O-acetyl- α -D-glucopyranosyl bromide. Treatment of the reaction mixture with moist ether and silver oxide converts both of these compounds into 2,3,4,6-tetra-O-acetyl-D-glucopyranoside is treated with bromine. It is suggested that the α -bromobenzyloxy group at C-1 can be displaced by a bromide ion to form 2,3,4,6-tetra-O-acetyl-D-glucopyranosyl bromide.

$$\begin{array}{rcl} \text{R-O-CHBr-Ph + Br^{-} \longrightarrow RBr + Ph-CHBr-O^{-}} \\ \downarrow \\ \text{Ph-CHO + Br^{-}} \end{array}$$

When bromine was added in smaller increments to a solution of 6 in benzene, a different set of products was produced. T.l.c. showed a compound believed to be the α -bromobenzyl glycoside, another compound believed to be the stable 2,3,4,6-tetra-O-acetyl- α -D-glucopyranosyl bromide, and a third compound which might have been the unstable 2,3,4,6-tetra-O-acetyl- β -D-glycopyranosyl bromide or the orthoacetate formed from it. Thus, the products that were formed appeared to be dependent upon the concentration of bromine, an observation which supports the proposed mechanism. Anomerization of 2,3,4,6-tetra-O-acetyl-D-glucopyranosyl bromide might have occurred in the presence of bromide ion.

The data presented here do not support the 4-centered transition-state mechanism¹⁰. With this mechanism operative, the α -D and β -D anomers of benzyl 2,3,4,6-tetra-O-acetyl-D-glucopyranoside should have produced exclusively only the corresponding α -D or β -D anomer of 2,3,4,6-tetra-O-acetyl-D-glucopyranosyl bromide, although anomerization after formation is not exluded.

Examination of the reaction of 6 with bromine was made with an e.p.r. spectrometer. While the reaction proceeded normally during the recording of spectra, no free radicals were detected; again, this may be due to low radical concentration or more likely to a short half-life of the radicals on the e.p.r. time-scale, or both.

In the case of reaction of 2,3,4,6-tetra-O-acetyl- α -D-glucopyranosylbenzene (8) with bromine, the methylene hydrogen is also the C-1 hydrogen atom of the glucopyranose ring. Abstraction of this hydrogen atom by a free radical would place a free radical on the ring. At -30° , the reaction of bromine with 8 under free-radical conditions produced only one compound as shown by t.l.e. It is speculated that this compound may have been 2,3,4,6-tetra-O-acetyl-1-bromo-1-deoxy-1-phenyl-D-glucopyranose (2,3,4,6-tetra-O-acetyl-1-phenyl-D-glucopyranosyl bromide). Efforts to isolate or derivatize this compound were unsuccessful, as it decomposed. Reaction of 8 with bromine at room temperature produced a mixture of at least 11 compounds as shown by t.l.e. It is possible that the first-formed product decomposed producing several compounds. The fact that 2,3,4,6-tetra-O-acetyl- β -D-glucopyranosylbenzene did react with bromine indicates that a free radical can be formed at C-1 of the glucopyranose ring, not an unlikely occurrence^{11,12}.

Di-*tert*-butyl peroxide did not produce any detectable reaction when it was used in place of bromine or chlorine in any of these reactions. This may be due in part to steric hindrance to the approach to the *tert*-butoxy radical.

With this method, it was not possible to form free radicals at C-2, C-3, C-4, or C-6 of the D-glucopyranose ring. Neither was there any evidence for the formation of free radicals at C-1 of the D-glucopyranose ring during the reactions of benzyl 2,3,4,6-tetra-O-acetyl- α -D-glucopyranoside and the corresponding β -D anomer with bromine and chlorine.

Hence, a great stability of α -bromobenzyl ethers of carbohydrates has been demonstrated. Only when the α -bromobenzyloxy group was at C-1 (α -bromobenzyl glycoside) was any further reaction demonstrated. Here, as the reaction was dependent on the concentration of bromine and formed a glycosyl bromide, it is speculated that the subsequent reaction was a nucleophilic displacement of the α -bromobenzyloxy group by bromide ion.

As the debenzylated carbohydrates were recovered with no changes in configuration, it must be assumed that there was no cleavage of the carbohydrate carbonoxygen bond. This assumption is in agreement with literature reports that indicate that an atom having sp² geometry does not easily form on the pyranoid ring¹³. Many instances of carbohydrate free-radicals have been reported. Cotton cellulose I and II subjected to γ -irradiation with ⁶⁰Co yielded stable free radicals¹⁴. Cellulose I gave a 3 line e.p.r. spectrum that probably resulted from removal of a hydrogen atom at C-5, and cellulose II gave a 5-line e.p.r. spectrum probably resulting from the summation of two free-radical spectra, one at C-5 and the other at C-6 arising from the removal of an OH group or a hydrogen atom. Similar results with cotton cellulose subjected to γ -irradiation have been reported by others^{15,16}.

Irradiation of solid α -D-glucopyranose by ⁶⁰Co followed by dissolution in water yielded carbon dioxide; paper chromatography showed seven additional compounds that were not identified¹⁷. In addition, ⁶⁰Co irradiation has been shown to produce hydrogen and carboxyl groups¹⁸. Upon γ -irradiation from ⁶⁰Co, α -D-glucose produced a 3-line e.p.r. spectrum, probably from $-CH_2 \cdot$ at C-6 or \cdot C-CH₂OH at C-5 with a single-line spectrum superimposed¹¹. It was suggested that the single-line spectrum was due to a radical associated with the ring structure.

Why the reaction proceeds differently with carbohydrate benzyl ethers than with alkyl benzyl ethers has not been established, but there is the possibility that the alkyl bromide is not formed from alkyl benzyl ethers by radical decomposition as proposed by Huang⁵⁻⁸ and Lovins^{2,3} but by nucleophilic displacement, and that this displacement is unfavorable with carbohydrates.

The evidence presented here indicates that chlorodeoxy or bromodeoxy sugars cannot be made by this reaction but that glycosyl bromides and chlorides can. From the same evidence, it can be deduced that this reaction cannot be used to generate free radicals on a glycosyl residue of a polysaccharide for graft polymerization but that the methylene carbon atom of a benzyl ether substituent on a polysaccharide is a potential site for initiation of polymerization.

EXPERIMENTAL

Benzyl ether derivatives. — Methyl 2,3,4,6-tetra-O-benzyl- α -D-glucopyranoside (1) was prepared by the method of Tate and Bishop¹⁹. Methyl 2,3-di-O-benzyl- α -D-glucopyranoside (2) was prepared by the method of Bell and Lorber²⁰. 6-O-Benzyl-D-glucopyranose (3) was prepared by the method of Anet²¹ from 6-O-benzyl-3,5-O-benzylidene-1,2-O-isopropylidene- α -D-glucofuranose²² (4).

Benzyl α,β -D-glucopyranoside (5) was prepared by the method of Wing and BeMiller²³. Benzyl 2,3,4,6-tetra-O-acetyl- α -D-glucopyranoside (6) was prepared by acetylation²⁴ of 5 and crystallization of the product from hot ethanol²⁵ to yield almost pure 6; m.p. 109°, lit.²⁵ m.p. 109.5–110.5°. T.I.c. examination of the product revealed a trace amount of the β -D anomer. Benzyl 2,3,4,6-tetra-O-acetyl- β -D-glucopyranoside (7) was prepared by the method of Piel and Purves²⁵.

Tetra-O-acetyl- α -D-glucopyranosylbenzene (8) was prepared by the method of Bonner²⁶.

General. - Solvents used were reagent- or analytical reagent-grade and were

dried by an appropriate procedure before use. Reactions were accomplished with the exclusion of moisture to the extent possible with normal precautions. Irradiation of the reaction mixtures was accomplished with incandescent bulbs.

Formation of benzaldehyde was determined by i.r. spectrophotometry and by formation of its (2,4-dinitrophenyl)hydrazone.

Alkaline hydrolysis was effected by shaking the organic solvent with saturated calcium hydroxide solution for 15 min, neutralization with carbon dioxide, and filtration¹.

Products were analyzed by t.l.c. on plates spread with Silica Gel H (Brinkmann Instruments Inc., Westbury, N.Y.) and developed with one of the following irrigants: (A) 9:6:3:1 (v/v) 1-butanol-acetic acid-ether-water, (B) 9:1 (v/v) benzene-acetone (both dried). After development, the plates were sprayed with 50% sulfuric acid in ethanol and charred.

Treatment of 1 with di-tert-butyl peroxide. — Methyl 2,3,4,6-tetra-O-benzyl- α -D-glucopyranoside (1, 0.1630 g, 0.29 mmole) was dissolved in 50 ml of carbon tetrachloride in an open, tall-form beaker, and 0.2 ml of di-tert-butyl peroxide was added to the solution, which was irradiated from above for 2 h with a 150-W bulb. A sample of the reaction mixture was treated with aqueous (2,4-dinitrophenyl)hydrazine reagent. No reaction occurred. Bromine (0.1 ml, 1.95 mmole) was then added whereupon hydrogen bromide immediately issued from the beaker. After the bromine, color had disappeared, the amorphous precipitate was subjected to alkaline hydrolysis. The hydrolysis products were determined by t.l.c. with irrigant A; methyl α -D-glucopyranoside and incompletely debenzylated compounds were present.

Treatment of 2 with bromine, chlorine, and di-tert-butyl peroxide. — Methyl 2,3-di-O-benzyl- α -D-glucopyranoside (2, 1.87 g, 5 mmole) was dissolved in 100 ml of benzene in a 250-ml, round-bottomed flask equipped with a reflux condenser, a nitrogen inlet tube, and a stoppered neck for introduction of bromine. The flask and condenser were then wrapped completely with aluminum foil to keep out light, and 0.5 ml (9.8 mmole) of bromine was added. After 5 h at room temperature, no detectable hydrogen bromide had formed. The aluminum foil was then removed, and hydrogen bromide began to be evolved. A 150-W bulb was positioned to shine on the flask. Aliquots taken from the flask as the reaction proceeded were treated with aqueous (2,4-dinitrophenyl)hydrazine reagent. A gummy residue formed on the inside of the flask during the reaction. When the bromine color had disappeared, the flask was stoppered and refrigerated overnight. The sample was then warmed to room temperature, and an aliquot of the supernatant and a portion of the gummy precipitate were treated separately with (2,4-dinitrophenyl)hydrazine reagent. Only the precipitate gave rise to benzaldehyde (2,4-dinitrophenyl)hydrazone. The remaining precipitate was subjected to alkaline hydrolysis. The hydrolysis product was determined by t.l.c. with irrigant A; methyl α -D-glucopyranoside was indicated.

Another portion of 2 was treated with bromine in benzene, and the precipitate that formed was mulled with Nujol and examined on cesium bromide plates with a

Beckman IR-10 spectrophotometer. A peak at 600 cm^{-1} , indicative of a carbon-bromine bond, was present.

A third portion of 2 (1.00 g, 2.69 mmole) was dissolved in 50 ml of chloroform in a round-bottomed flask. Chlorine gas was bubbled slowly into the solution during irradiation with a 150-W bulb until a light yellow color was permanent. The chloroform was removed under diminished pressure, and the syrupy residue was exposed to room air for about 1 month. The amorphous solid which formed was recrystallized from absolute ethanol yielding a white compound; m.p. 166° [lit.¹ m.p. 164–165°]. The m.p. did not change on admixture with an authentic sample of methyl α -D-glucopyranoside.

A fourth portion of 2 (0.500 g, 1.34 mmole) was dissolved in 10 ml of chloroform and reacted with 0.3 ml of di-*tert*-butyl peroxide in a stoppered flask for 2 weeks with periodic irradiation from a 150-W bulb. No reaction was indicated either by treatment with aqueous 2,4-dinitrophenylhydrazine reagent or on examination by t.l.c. using irrigant A.

Treatment of 3 with bromine. — 6-O-Benzyl-D-glucose (3) (1.00 g, 3.69 mmole) was dissolved in 50 ml of benzene in a tall-form beaker. Bromine (0.1 ml, 1.95 mmole) was added, and the reaction mixture was irradiated from above with a 60-W bulb. A gentle stream of dry nitrogen was used to sweep hydrogen bromide from the beaker. After 1 h and 2 h, additional 0.1-ml portions of bromine were added, and the reaction was continued for an additional h. A syrupy residue formed, and the supernatant was decanted to recover the residue. An aliquot of the supernatant solution and a portion of the residue were treated with aqueous (2,4-dinitrophenyl)hydrazine reagent; the latter but not the former gave benzaldehyde (2,4-dinitrophenyl)hydrazone. The remaining residue was subjected to alkaline hydrolysis, and the hydrolysis product was determined by t.l.c. with irrigant A; only D-glucose was present.

Treatment of 4 with bromine. — 6-O-Benzyl-3,5-O-benzylidene-1,2-O-isopropylidene- α -D-glucofuranose (4, 1.00 g, 2.5 mmole) was dissolved in 50 ml of benzene in a tall-form beaker. Bromine (0.1 ml, 1.95 mmole) was added, and the solution was irradiated from above with a 150-W bulb. After 1 h and 2 h, additional 0.1 ml portions of bromine were added, and the reaction was continued for a total of 3 h. A syrupy precipitate that formed was subjected to alkaline hydrolysis. The hydrolysis product was determined by t.l.c. with irrigant A; only D-glucose was found in the reaction mixture.

Treatment of 5 with bromine. — Benzyl α,β -D-glucopyranoside (5) (0.500 g, 1.84 mmole) was dissolved in 50 ml of chloroform in a tall-form beaker, and 0.2 ml (3.9 mmole) of bromine was added. The sample was irradiated from above with a 150-W bulb, and a gentle stream of dry nitrogen was used to sweep hydrogen bromide from the beaker. A syrupy residue quickly formed and, after 1 h, was isolated by decanting the supernatant and subjected to alkaline hydrolysis. The product was determined by t.l.c. with irrigant A; only D-glucose was found as a product.

Treatment of 6 and 7 with bromine and chlorine. — Benzyl 2,3,4,6-tetra-O-acetyl- α -D-glucopyranoside (6) (2.00 g, 4.56 mmole) was dissolved in 50 ml of benzene in a

round-bottomed flask equipped with a reflux condenser and a nitrogen inlet tube. Bromine (0.5 ml, 9.8 mmole) was added, and a 75-W spotlight bulb was positioned to just touch the flask. An aluminum-foil reflector was placed on the opposite side of the flask; the heat from the bulb caused refluxing. After 2 h, an additional 0.1 ml (1.95 mmole) of bromine was added to ensure complete reaction. No residue formed during the bromination reaction. An hour later, the reaction mixture was concentrated to a syrup under diminished pressure. The syrup was treated with moist ether and silver carbonate; the reaction product corresponded to authentic 2,3,4,6tetra-O-acetyl-D-glucose upon t.l.c. with irrigant B.

Another solution containing 1.00 g (2.28 mmole) of 6 in 10 ml of carbon tetrachloride was cooled to -30° in a Dry Ice-acetone bath, and 0.12 ml (2.3 mmole) of bromine was added. The mixture was carefully irradiated with a 75-W spot-light bulb until the bromine color disappeared. The sample was then allowed to warm to room temperature, and the volume was decreased by passing a stream of dry nitrogen over the surface of the sample. The concentrated solution was examined by t.l.c. with irrigant *B*; 2 components were present, one corresponding to the starting material and one believed to be the α -bromobenzyl glycoside. The solution was also examined by i.r. spectrophotometry with cesium bromide plates in a Beckman IR-10 spectrophotometer; a medium-strength peak at 600 cm⁻¹, indicative of a carbon-bromine bond was found.

To another solution of 2.00 g (4.56 mmole) of 6 in 50 ml of benzene in a 100-ml flask, bromine (0.01 ml, 0.195 mmole) was added, and the sample was irradiated with a 74-W bulb. As the bromine color disappeared, additional 0.01-ml portions of bromine were added until the solution remained slightly colored. The reaction mixture was examined by t.l.c. with irrigant B. One of the three compounds present had an R_F value corresponding to that of 2,3,4,6-tetra-O-acetyl- α -D-glucopyranosyl bromide. Another compound present in lesser quantity might have been the β -D anomer or the orthoacetate. The third compound was believed to be the α -bromobenzyl glycoside. None of the products were positively identified. Removal of the solvent under diminished pressure followed by reaction of the residue with moist ether and silver carbonate converted all three compounds into 2,3,4,6-tetra-O-acetyl-D-gluco-pyranose, as determined by t.l.c. with irrigant B.

Into a solution of 2.00 g (4.56 mmole) of 6 in 50 ml of benzene in a 100-ml flask, chlorine gas was bubbled very slowly until the solution remained slightly colored. Irradiation of the sample was provided by a 75-W spot-light bulb during the reaction. The reaction mixture was concentrated to a syrup under diminished pressure. Removal of the solvent and treatment with moist ether and silver carbonate again gave only 2,3,4,6-tetra-O-acetyl-D-glucopyranose.

Benzyl 2,3,4,6-tetra-O-acetyl- β -D-glucopyranoside (7) (1.0 g, 1.57 mmole) was dissolved in 50 ml of chloroform in a 100-ml, round-bottomed flask equipped with a reflux condenser and a nitrogen inlet tube. Bromine was added in 0.1-ml (1.95-mmole) increments until a slight bromine color remained, and the reaction mixture was irradiated with a 150-W bulb. Hydrogen bromide was swept from the flask with a

slow stream of dry nitrogen. Removal of the solvent and treatment with moist ether and silver carbonate again yielded only 2,3,4,6-tetra-O-acetyl-D-glucopyranose.

Reaction of 7 with chlorine under similar conditions gave the same product.

Treatment of 8 with bromine. — Tetra-O-acetyl- β -D-glucopyranosylbenzene (8) (1.00 g, 2.44 mmole) was dissolved in 50 ml of benzene in a round-bottomed flask equipped with a reflux condenser and a nitrogen inlet tube. Bromine (0.5 ml, 9.8 mmole) was added, and the sample was irradiated with a 75-W spot-light bulb. After 1 h, the bromine color disappeared, and the reaction mixture was examined by t.l.c. with irrigant B; a single, unstable compound was found as the product.

A solution of 1.00 g (2.44 mmole) of 8 in 10 ml of carbon tetrachloride was cooled to -30° in a Dry Ice-acetone bath. Bromine (0.12 ml, 2.34 mmole) was added, and the mixture was carefully irradiated with a 75-W spot-light bulb. After 20 min, the bromine color had disappeared. The reaction mixture was examined by t.l.c. with irrigant *B*; at least 11 compounds were present.

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