of the velocity controlling step, the higher the ion charge the slower the exchange.[3]

(3) This document is based on work performed for the Atomic Energy Project at Oak Ridge National Laboratory.

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The Nitration and Bromination of Tetraacetyl-β-D-glucopyranosylbenzene

BY JAMES M. CRAIG AND WILLIAM A. BONNER

While tetraacetyl-β-D-glucopyranosylbenzene (I) and related compounds have been known for several years[1] and the α-anomer of I has been discovered recently,[2] the chemical reactions of these compounds have been limited so far to those characteristic of the glycosyl side chain. The potentially more significant reactions of the aromatic nucleus, which might lead to series of aromatic derivatives possessing stable, water-soluble side chains of high molecular weight, have not yet been explored. In this note we wish to report the application of two typical aromatic-type reactions, nitration and bromination, to the benzene nucleus of I.

When I, dissolved in a mixture of acetic acid and acetic anhydride, was warmed with cupric nitrate, nitric oxide was evolved and the nitration mixture yielded a yellow sirup from which *p*-(tetraacetyl-β-D-glucopyranosyl)-nitrobenzene(II) m. p. 165–165.5°, $[\alpha]^{28}\mathrm{D}$ − 40.3°, could be isolated in 22% yield. The structure of II was established by oxidation to *p*-nitrobenzoic acid. II could be deacetylated readily to *p*-(β-D-glucopyranosyl)-nitrobenzene, m. p. 181.5–182.5°, $[\alpha]^{25}\mathrm{D}$ 22.6°. The mother liquors from which II was obtained yielded a yellow glass, $[\alpha]^{28}\mathrm{D}$ 60.5°, on evaporation. This produced only a trace of *p*-nitrobenzoic acid on oxidation, and no other isolable product. The high positive rotation of this glass and the failure to isolate an aromatic acid on its oxidation, suggest that the nitration was accompanied by considerable degradation, since pure I was the starting material. When the usual mixture of nitric and sulfuric acids was employed in the nitration of I a glass, $[\alpha]^{27}\mathrm{D}$ 45.4°, was obtained, but this yielded only traces of a high melting solid product, and its oxidation similarly yielded only minute amounts of substances which appeared to be *o*- and *p*-nitrobenzoic acids.

Attempts to brominate I in acetic acid or chloroform, either at room or reflux temperatures, were unsuccessful. When I was dissolved in bromine containing fused ferric chloride and allowed to stand seven hours, the product was a yellow glass. By reacetylation and crystallization from 2-propanol 1-(tetraacetyl-β-D-glucopyranosyl)-3,4-dibromobenzene (III), m. p. 164.5–165°, $[\alpha]^{30}\mathrm{D}$ −29.0°, could be obtained. Its structure was substantiated by oxidation to 3,4-dibromobenzoic acid. The mother liquors producing III yielded a second crop of crystalline material, m. p. 105–108°, $[\alpha]^{24}\mathrm{D}$ −28.8°, on concentration. This material appeared to be a mixture of III and *p*-(tetraacetyl - β - D - glucopyranosyl) - bromobenzene (IV). When the above bromination was conducted for about three hours instead of seven, the product was approximately the same mixture of III and IV. It was not possible to separate this mixture into its components by recrystallization from 2-propanol, but its composition was supported by analysis and oxidation to *p*-bromo- and 3,4-dibromobenzoic acids.

Experimental Part

***p*-(Tetraacetyl-β-D-glucopyranosyl)-nitrobenzene (II).**—The nitrating reagent was prepared by adding cupric nitrate trihydrate (40 g., 0.165 mole) to a mixture of acetic anhydride (56 ml.) and acetic acid (24 ml.). To this reagent was slowly added tetraacetyl-β-D-glucopyranosylbenzene (8.0 g., 0.0196 mole) dissolved in a mixture of acetic anhydride (48 ml.) and acetic acid (32 ml.). The temperature of the reaction mixture was raised from an initial 40 to 50° on the water-bath, causing a gentle evolution of nitric oxide. After twenty minutes the reaction was cooled and poured into one liter of ice-water, and the aqueous solution allowed to stand for four hours. The viscous, dark amber gum which precipitated was dissolved in ether (50 ml.) and the aqueous solution extracted five times with 50-ml. portions of ether. The combined ether solutions were washed with small portions of cold water, cold, saturated sodium bicarbonate solution, and finally with cold water. The clear ether solution, dried over anhydrous sodium sulfate, was evaporated to give 9.1 g. of a yellow, semi-crystalline glass. This was crystallized from 2-propanol to yield two crops of yellow solid: 0.34 g., m. p. 151–156°, and 1.95 g., m. p. 155–161°. These were combined and recrystallized twice to yield 1.94 g. (21.9%) of pure *p*-(tetraacetyl-β-D-glucopyranosyl)-nitrobenzene, m. p. 165–165.5°, $[\alpha]^{28}\mathrm{D}$ −40.3° (*c*, 2.284, chloroform).

Anal. Calcd. for $C_{20}H_{23}O_{11}N$: C, 52.98; H, 5.11; N, 3.09. Found: C, 53.31; H, 5.15; N, 3.26, 3.23.

A 78-mg. sample of the pure material was oxidized with alkaline potassium permanganate to produce *p*-nitrobenzoic acid, m. p. 237–239°, mixed m. p. with an authentic sample 236–237°.

The original 2-propanol mother liquors were concentrated to dryness leaving a yellow glass, $[\alpha]^{28}\mathrm{D}$ 60.5° (chloroform), from which further crystalline material could not be isolated. An alkaline permanganate oxidation of 1.0 g. of this glass produced only a trace of *p*-nitrobenzoic acid, and no other solid product was recovered.

***p*-(β-D-Glucopyranosyl)-nitrobenzene.**—*p*-(Tetraacetyl-β-D-glucopyranosyl)-nitrobenzene (0.50 g.) was dissolved in methanol (25 ml.) saturated with ammonia (14.6 g. of NH_3 in 100 ml.). The solution stood for twenty-four hours, then was evaporated to dryness. The yellow crystalline residue was extracted several times with warm absolute ether to remove acetamide. The remaining crystalline residue (0.34 g.) was recrystallized from ethyl acetate to give pure *p*-(β-D-glucopyranosyl)-nitrobenzene in the form of light yellow platelets, m. p. 181.5–182.5°, $[\alpha]^{25}\mathrm{D}$ 22.6° (*c*, 1.24, methanol).

Anal. Calcd. for $C_{12}H_{15}O_7N$: C, 50.52; H, 5.30; N, 4.91. Found: C, 50.42, 50.65; H, 5.47, 5.56; N, 4.95, 5.05.

Acetylation of 64 mg. of the pure material with acetic

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(1) Hurd and Bonner, THIS JOURNAL, 67, 1664, 1759, 1972, 1977 (1945).

(2) Bonner and Craig, *ibid.*, 72, 3480 (1950).

anhydride containing a trace of sulfuric acid produced 76 mg. of crystalline material identical with the original *p*-(tetraacetyl-β-D-glucopyranosyl)-nitrobenzene.

1-(Tetraacetyl-β-D-glucopyranosyl)-3,4-dibromobenzene (III).—Tetraacetyl-β-D-glucopyranosylbenzene (5.0 g.) was dissolved in bromine (25 ml.) and powdered, freshly fused ferric chloride (0.5 g.) was added. The flask was protected with a calcium chloride tube and the reaction mixture allowed to stand for four hours at room temperature. The bulk of the excess bromine was removed in three hours with a stream of dry air, leaving a dark red viscous gum which was dissolved in chloroform (100 ml.). The chloroform solution was washed with saturated aqueous solutions of sodium bisulfite and sodium bicarbonate, and finally with water. After drying over calcium chloride the chloroform was distilled to leave 5.1 g. of light yellow glass. This was treated with acetic anhydride (40 ml.) and a drop of sulfuric acid. The yellow glass recovered by processing the acetylation mixture in the usual manner did not crystallize and was acetylated again. The product obtained was a thick sirup which partially crystallized. This was recrystallized from 2-propanol to yield 1.29 g. of white needles, m. p. 124.5–132.5°. Six additional recrystallizations from the same solvent gave 0.32 g. of pure 1-(tetraacetyl-β-D-glucopyranosyl)-3,4-dibromobenzene, m. p. 164.5–165°, $[\alpha]^{30}\text{D}$ −29.0° (*c*, 2.893, chloroform).

Anal. Calcd. for $C_{20}H_{22}O_9Br_2$: C, 42.42; H, 3.92; Br, 28.23. Found: C, 42.68; H, 4.03; Br, 28.40, 28.28.

An alkaline potassium permanganate oxidation of 87 mg. of the pure product gave 59 mg. of white solid, m. p. 228–234°. This was sublimed at reduced pressure to give pure 3,4-dibromobenzoic acid, m. p. 235–237°, mixed m. p. with an authentic sample[3] 235–237°.

On concentration of the original mother liquors there was obtained additional crystalline material, m. p. 105–108°, $[\alpha]^{25}\text{D}$ −28.8° (*c*, 0.555, chloroform). This could not be purified by further recrystallization, and was apparently identical with the mixture described below.

The procedure described above was repeated using 4.0 g. of starting material and reducing the reaction time to 3.25 hours. The colorless sirup obtained was recrystallized from 2-propanol to yield 1.65 g. of product, m. p. 104–110°. Several more recrystallizations resulted in an apparently pure product, m. p. 111.5–112.5°. Oxidation of 0.20 g. of this material with alkaline permanganate solution produced 0.11 g. of crystals, m. p. 237–247° after two recrystallizations from a mixture of ethanol and water. Sublimation of this product gave two fractions, m. p. 246–249° and m. p. 234–245°. The first fraction gave a mixed m. p. of 249.5–251.5° with pure *p*-bromobenzoic acid, m. p. 251–253°. The second fraction was impure 3,4-dibromobenzoic acid as seen from the oxidation described below.

The crystalline product, m. p. 111.5–112.5°, was treated with acetic anhydride and a trace of sulfuric acid, but was recovered unchanged, m. p. 111.5–112.5, $[\alpha]^{26}\text{D}$ −29.6° (*c*, 2.67, chloroform). It analyzed for an approximately equimolar mixture of III and *p*-(tetraacetyl-β-D-glucopyranosyl)-bromobenzene (IV).

Anal. Calcd. for $C_{20}H_{23}O_9Br$: C, 49.29; H, 4.75; Br, 16.40. Calcd. for $C_{20}H_{22}O_9Br_2$: C, 42.42; H, 3.92; Br, 28.23. Calcd. for $C_{40}H_{45}O_{18}Br_3$: C, 45.6; H, 4.32; Br, 22.8. Found: C, 46.88; H, 4.49; Br, 21.43.

Oxidation of this product with permanganate was repeated as before to yield a crystalline solid, m. p. 232–233°, which did not depress the m. p. of 3,4-dibromobenzoic acid, m. p. 235–236°.

The original mother liquors were concentrated to dryness leaving 1.28 g. of yellow sirup which produced no further crystalline material.

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[3] Neville and Winther, *Ber.*, **13**, 962 (1880).

Synthesis of Aromatic Fluorides through Diazotization in Anhydrous Hydrogen Fluoride

BY RICHARD L. FERM[1] AND CALVIN A. VANDERWERF

Although fluorobenzene was obtained from aniline by the preparation and decomposition of benzenediazonium fluoride in anhydrous hydrogen fluoride as early as 1934,[2] the general applicability of this method for the synthesis of aromatic fluorides has not been investigated. Our studies have shown that this procedure is successful in many cases, and that, because of its simplicity, it is often preferable to the methods commonly used[3] for the synthesis of aromatic fluorides.

The following compounds were prepared successfully by this method in the percentage yields indicated: fluorobenzene (87), *o*-fluorotoluene (73), *m*-fluorotoluene (82), *p*-fluorotoluene (78), 4-fluoro-1,3-dimethylbenzene (57), 2-fluoro-1,4-dimethylbenzene[4] (43), *m*-fluorochlorobenzene (81), *p*-fluorochlorobenzene (74), *m*-nitrofluorobenzene (39), *p*-nitrofluorobenzene (62), *m*-fluorophenol (46) *o*-fluorobenzoic acid (57), *m*-fluorobenzoic acid (78), *p*-fluorobenzoic acid (98) and *o*-fluorodiphenyl (82).

In many cases, the yields of fluorides are approximately as good or better than those reported[5] for the same compounds by the familiar Schiemann method, in which the diazonium fluoborates are isolated and thermally decomposed. It is noteworthy that the three fluorobenzoic acids and *m*-fluorophenol can be prepared directly from the corresponding amines, in contrast to results obtained by use of the Schiemann reaction. Similarly, the yield of *o*-fluorotoluene is considerably better than that obtained by the latter method.[6]

The following amines, all of which are substituted in the ortho position with groups which contain one or more atoms with unshared electron pairs, failed to give satisfactory yields of fluorides: *o*-chloroaniline, *o*-nitroaniline, *o*-aminophenol and *o*-anisidine. In each of these cases little nitrogen was evolved during the attempted decomposition of the corresponding diazonium fluoride, and failure of the synthesis apparently resulted from the fact that the diazonium salt was not decomposed at the highest temperature obtainable in anhydrous hydrogen fluoride under reflux at atmospheric pressure. Attempted decomposition of the diazonium fluorides at higher temperatures

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[1] Department of Chemical Engineering, University of New Mexico, Albuquerque.

[2] Osswald and Scherer, German Patent 600,706, July 30, 1934 [*C. A.*, **28**, 7260 (1934)].

[3] See Bockemüller, "Organische Fluorverbindungen," Ferd. Enke, Stuttgart, 1936, pp. 54–66.

[4] M. p. −6°. *Anal.* Calcd. for C_8H_9F: C, 77.4; H, 7.3. Found: C, 77.4; H, 7.4.

[5] For a summary, see Bockemüller in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, p. 246.

[6] Workers in this Laboratory have consistently obtained very low yields of *o*-fluorotoluene following Schiemann's directions.