1,3:5,7-Dimethylene-D,L-perseitol.—A solution of equal amounts of the enantiomorphs in fifty parts of hot 80% ethanol deposited fine needle-like crystals which melted at 236–237° and showed no rotation in aqueous solution. The substance is a hemihydrate which becomes anhydrous when heated at 120° *in vacuo* for some hours. The hemihydrate crystals obviously represent a true racemate. The anhydrous material also melts at 236–237°; apparently the water of crystallization leaves the hemihydrate before the substance melts.

Anal. Calcd. for $C_9H_{16}O_7\cdot{}^1/_2H_2O$: C, 44.08; H, 6.99; H_2O, 3.67. Found: C, 43.90; H, 7.08; H_2O, 3.59.

Calcd. for $C_9H_{16}O_7$ (anhydrous): C, 45.76; H, 6.83. Found: C, 45.91; H, 6.83.

The racemic character of 1,3:5,7-dibenzylidene- and 1,3:5,7-dimethylene-D,L-perseitols was verified by determination of their optical-crystallographic properties by Mr. George L. Keenan. The data for the compounds and their component optically active forms are compiled in Table I.

TABLE I

OPTICAL-CRYSTALLOGRAPHIC PROPERTIES OF THE 1,3:5,7-DIBENZYLIDENE- AND 1,3:5,7-DIMETHYLENE PERSEITOLS

	Dibenzylidene perseitol		Dimethylene perseitol	
	D or L	D,L	D or L	D,L-hemihydrate
$n\alpha$	1.567[a]	1.583[a]	1.515[a]	1.530[a]
$n\beta$	1.615[b]	1.613[b]	1.535[b]	Indeterminate
$n\gamma$	1.625	1.637[b]	1.540[b]	1.530[b]
Elongation	Negative	Negative	Negative	Negative
Extinction	Parallel and inclined	Parallel	Parallel	Parallel and inclined
M. p., °C.	280	271	251	236

[a] Shown lengthwise. [b] Shown crosswise. All the substances crystallize as rods. The refractive indices are for ordinary light at 25° and are ±0.002.

Summary

Proof is presented that dibenzylidene-D-perseitol (dibenzylidene-D-manno-D-*gala*-heptitol) is the 1,3:5,7-dibenzylidene diacetal. Neither it nor the trimethyl-D-perseitol which is obtained by its methylation and hydrolysis is oxidized by sodium periodate and the absence of α-glycol groupings in this related pair of compounds limits the structure of the diacetal to that of 1,3:5,7-dibenzylidene-D-perseitol and that of the derived trimethyl-heptitol to 2,4,6-trimethyl-D-perseitol.

The condensation of D-perseitol with formaldehyde yields a diacetal which must be 1,3:5,7-dimethylene-D-perseitol since its trimethyl derivative is identical with the compound formed by methylenation of 2,4,6-trimethyl-D-perseitol.

The enantiomorphous 1,3:5,7-dibenzylidene- and 1,3:5,7-dimethylene-L-perseitols have been prepared from D-gala-L-*manno*-heptitol and they combine with the D-forms to form true racemate crystals.

BETHESDA, MARYLAND RECEIVED SEPTEMBER 29, 1947

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

The Cleavage of Tetraacetyl-β-D-thioglucosides with Bromine in Acetic Acid[1]

BY WILLIAM A. BONNER

Several years ago it was shown[2] that phenyl tetraacylglucosides were brominated quantitatively when treated with excess bromine in glacial acetic acid. That bromination occurred at the *para* position was shown by hydrolysis of the glucoside and isolation of the brominated aglucone, *p*-bromophenol. In this respect the phenyl glycosides, which are cyclic acetals, resemble true phenyl alkyl ethers such as anisole.

It seemed desirable to extend this reaction to the phenyl polyacylthioglycosides, and to determine whether these undergo similar *para*-bromination. Such was anticipated, since aromatic thioethers are known[3] to undergo nuclear halogenation with readiness. In addition, adducts of bromine to the sulfur atom of the thioglycoside were considered likely, since halogens have been shown[4] to add readily to organic sulfides to form what are presumably halo sulfonium halides.

When phenyl tetraacetyl-β-D-thioglucoside in glacial acetic acid was treated with about thirteen equivalents of bromine and permitted to stand at room temperature for several hours, a white, crystalline material was isolated. On recrystallization pure α-D-glucose pentaacetate was obtained. The crude reaction product was not pure α-D-glucose pentaacetate, however, since its specific rotation (88.5 to 91.7°, depending upon reaction conditions) and its melting point (98–103°) were somewhat below those for the pure substance. The presence of small quantities of the β-anomer may explain these low values, as well as the presence of other impurities. The crude material, however, was substantially α-D-glucose pentaacetate, since this was obtained in reasonable purity on one or two recrystallizations. Based on pentaacetate the yield of crude product varied between 75 and 81%, depending upon reaction conditions.

This striking and unexpected reaction which involves cleavage of the acylated thioglucoside and replacement of the sulfur moiety with acetoxy was found to be quite general with respect to the thioaglucone. Both benzyl tetraacetyl-β-D-thioglucoside and ethyl tetraacetyl-β-D-thioglucoside produced α-D-glucose pentaacetate in comparable

---

[1] Presented before the Division of Sugar Chemistry and Technology of the American Chemical Society, New York, September, 1947.

[2] Hurd and Bonner, THIS JOURNAL, **67**, 1764 (1945).

[3] Bourgeois, *Ber.*, **28**, 2321 (1895); Böeseken and Waterman, *Rec. trav. chim.*, **29**, 321 (1910); Bourgeois and Abraham, *ibid.*, **30**, 418 (1911).

[4] Patein, *Bull. soc. chim.*, **50**, 201 (1888); Fries and Vogt, *Ann.*, **381**, 337 (1911); Chelintzev, *J. Russ. Phys.-Chem. Soc.*, **44**, 1885 (1913).

yields under similar conditions. Thus an aryl, an aralkyl, and an alkyl tetraacetyl-β-D-thioglucoside all showed identical behavior under the influence of bromine in acetic acid.

That bromine alone was responsible for the cleavage was shown by isolation of pure starting material in substantial yield when bromine was omitted from the reaction mixture, or when bromide ion (*i. e.*, lithium bromide) was substituted for bromine. Similarly, both hydrogen bromide and bromoacetic acid, other possible constituents of the reaction mixture, were found incapable of producing cleavage. Experiments designed to elucidate the mechanism of this unexpected cleavage of thioglucosides with bromine are currently in progress.

Under certain conditions bromine was found to have a labilizing effect on the acetyl functions of phenyl tetraacetyl-β-D-thioglucoside. Thus when the cleavage with bromine was attempted in methanol rather than acetic acid, the aqueous layer obtained during processing was dextro-rotatory, while the ether layer yielded only a small quantity of thin oil having a negligible rotation. Apparently bromine in methanol resulted in complete deacetylation. Similarly, when propionic acid was employed as solvent in the reaction, a sirup was isolated from which only minute quantities of indistinct crystalline materials were obtained. It is here probable that bromine engendered a partial replacement of the acetyl functions with propionyl, resulting in a substantially sirupy product. The deacetylating power of bromine in methanol was further demonstrated with α-D-glucose pentaacetate. When this substance was treated with bromine in methanol, permitted to stand several hours, and extracted with ether, optical activity was found in the aqueous layer while the ether layer was inactive. Similarly, when α-D-glucose pentaacetate was treated with bromine in propionic acid a sirup resulted, $[\alpha]^{25}\text{D}$ 51.4°. Since the rotation of this product is fairly close to that of equilibrated sirupy D-glucose pentapropionate,[5] it seems probable that bromine not only caused replacement of acetyl with propionyl, but also brought about anomerization. Although it is indicated that bromine may labilize acetyl groups in acetic acid medium, the medium seems to prevent extensive deacetylation, transacylation or anomerization from occurring. Thus bromine in acetic acid is without action on α-D-glucose pentaacetate. These effects of bromine on acylated carbohydrate derivatives are under more extensive study at the present time.

Experimental Part

Phenyl Tetraacetyl-β-D-thioglucoside and Bromine in Acetic Acid.—Phenyl tetraacetyl-β-D-thioglucoside (1.00 g.) was dissolved in glacial acetic acid (20 ml.) and bromine (1.5 ml., 12.8 equivalents) added. The mixture stood at room temperature for about three hours and was then poured into water (100 ml.). The cloudy red suspension was extracted twice with 60-ml. portions of ether. The ether extract was washed once with water, then with sodium bisulfite solution to remove free bromine, again twice with water, then with saturated sodium bicarbonate solution until gas evolution ceased, and again with water. After drying over anhydrous sodium sulfate and decanting, the solvent was distilled to yield 0.67 g. (75.5%) of a clear glass which crystallized spontaneously. After three recrystallizations from 2-propanol this material melted at 111.5°. It was shown to be α-D-glucose pentaacetate by mixed melting point with an authentic sample (m. p. 112–112.5°), 111–111.5°, and specific rotation $[\alpha]^{25}\text{D}$ 102.8° ($CHCl_3$; *c*, 4.047). The latter value is in agreement with $[\alpha]^{20}\text{D}$ 101.6° reported by Hudson and Dale.[6]

In a second experiment phenyl tetraacetyl-β-D-thioglucoside (1.00 g.) in acetic acid (10 ml.) was treated with bromine (1.5 ml.) and permitted to stand for about twenty-three hours. The reaction mixture was processed essentially as above to yield 0.72 g. (81.3%) of crude, solid product. This crude material showed $[\alpha]^{25}\text{D}$ 88.5° ($CHCl_3$; *c*, 2.535).

In a third experiment the thioglucoside (1.00 g.) in acetic acid (20 ml.) was treated with bromine (1.5 ml.) and allowed to stand for four hours. The crude product, a white solid, weighed 0.68 g. (76.8%). It melted from 98–103° with preliminary softening from 90°, and showed $[\alpha]^{25}\text{D}$ 91.7° ($CHCl_3$; *c*, 1.887).

Benzyl Tetraacetyl-β-D-thioglucoside and Bromine in Acetic Acid.—Benzyl tetraacetyl-β-D-thioglucoside (0.50 g., m. p. 97.5–98°, prepared by the method of Schneider, Sepp and Stiehler[7]) was dissolved in glacial acetic acid (10 ml.), and bromine (0.75 ml.) added. The mixture stood at room temperature for three and one-half hours, was poured into 50 ml. of water, and the product isolated and purified as before. On removal of the ether there resulted 0.48 g. (110%) of thick sirup which crystallized rapidly. After two recrystallizations from a mixture of 2-propanol and water there remained 0.13 g. (30%) of pure α-D-glucose pentaacetate, m. p. 111–111.5°; mixed m. p. with an authentic sample, 110–111°; $[\alpha]^{25}\text{D}$ 102.2° ($CHCl_3$; *c*, 0.920). A second crop (0.05 g.) was obtained from the mother liquors on standing overnight, m. p. 112°.

Ethyl Tetraacetyl-β-D-thioglucoside and Bromine in Acetic Acid.—Ethyl tetraacetyl-β-D-thioglucoside[7] (0.50 g.; m. p. 76.5–77.5°), acetic acid (10 ml.) and bromine (0.88 ml.) were mixed and permitted to stand for four hours. On processing in the usual fashion there resulted 0.46 g. (92%) of crude α-D-glucose pentaacetate. After two recrystallizations from dilute 2-propanol the material melted at 109.5–111°, and showed no melting point depression (110–111°) when mixed with an authentic sample.

Phenyl Tetraacetyl-β-D-thioglucoside and Bromine in Methanol.—Phenyl tetraacetyl-β-D-thioglucoside (1.5 g.) was placed in methanol (30 ml.) in which it was insoluble. On adding bromine (2.2 ml.) the thioglucoside dissolved immediately, and the solution stood for four hours. It was poured into dilute sodium bisulfite solution to decolorize, resulting in a completely clear solution in contrast to the cloudy suspensions previously obtained. The aqueous mixture was extracted twice with ether, and the extract washed as before. Distillation of the solvent resulted in 0.52 g. of a clear, malodorous oil which would not crystallize. This showed a minute rotation, $[\alpha]^{25}\text{D}$ 2.5° ($CHCl_3$; *c*, 4.040), compared with that of the previous crude products. The clear, aqueous layer remaining after the above ether extraction was found to be dextro-rotatory.

Phenyl Tetraacetyl-β-D-thioglucoside and Bromine in Propionic Acid.—The above experiment was duplicated using propionic acid (30 ml.) in place of methanol. There resulted 1.12 g. of amber sirup after customary processing. This product showed qualitative tests for sulfur and bromine. On standing it underwent partial crystallization. A seed was removed, and the remainder dissolved in 2-propanol (8 ml.). The solution was cooled, seeded and placed at 0°. Ten milligrams of solid, m. p. 88–91°, was

---

(5) Bonner, Hurd and Cantor, THIS JOURNAL, **69**, 1816 (1947).

(6) Hudson and Dale, *ibid.*, **37**, 1264 (1915).

(7) Schneider, Sepp and Stiehler, *Ber.*, **51**, 224 (1918).

isolated. The mother liquors were evaporated in an air stream to yield a solid. This was slurried with 2-propanol and filtered, giving a small quantity of crystals, m. p. 147–152°. The filtrate was kept at 0° for several weeks, resulting in *ca.* five milligrams of solid, m. p. 120–140°. No attempt was made to purify or identify these products, a complex mixture apparently having been obtained.

Phenyl Tetraacetyl-β-D-thioglucoside in Acetic Acid.—To be certain that bromine was essential for the cleavage reaction to take place, this constituent was omitted from one reaction mixture. The thioglucoside (1.00 g.) was dissolved in acetic acid (20 ml.) and the solution permitted to stand at room temperature for seventeen hours. The mixture was poured into water and the product isolated exactly as previously described. There resulted 1.01 g. of pure starting material, m. p. 117.5–118°; mixed m. p. 117–117.5°.

Phenyl Tetraacetyl-β-D-thioglucoside and Lithium Bromide in Acetic Acid.—To see if bromide ion was in any way responsible for the cleavage, lithium bromide was employed instead of bromine in one experiment. The thioglucoside (1.00 g.) was dissolved in acetic acid (5 ml.), and lithium bromide (0.59 g., 3 equivalents) was dissolved in acetic acid (4 ml.). The two solutions, cooled to room temperature, were mixed and diluted to 10 ml. Absence of reaction was observed by polarimetric observation, no mutarotation being noted during twenty-four hours. The mixture was poured into water and processed as usual, except that the bisulfite wash was omitted. There was recovered 0.95 g. (95%) of starting material, m. p. 117–117.5°, mixed m. p. 116.5–117.5°.

Phenyl Tetraacetyl-β-D-thioglucoside and Hydrogen Bromide in Acetic Acid.—The thioglucoside (0.61 g.) was dissolved in acetic acid and 32% hydrogen bromide in acetic acid (1.75 g., 5 equivalents of hydrogen bromide) added. The mixture was diluted to 100 ml. and observed polarimetrically. No mutarotation was noted during one hundred and eleven minutes. The mixture was poured into water, extracted with ether, and the product isolated as above. There resulted 0.55 g. (90%) of starting material, m. p. 117–118°, mixed m. p. 117–118°, $[\alpha]^{25}\text{D}$ −17.0° ($CHCl_3$; *c*, 1.587). Thus hydrogen bromide does not enter into the reaction mechanism in any direct manner. It is interesting to note that hydrogen bromide was also completely without action on phenyl tetraacetyl-β-D-glucoside under the same conditions, the starting material being recovered quantitatively.

Phenyl Tetraacetyl-β-D-thioglucoside, Bromoacetic and Acetic Acids.—Bromoacetic acid (1.58 g., 5 equivalents) was dissolved in acetic acid and diluted to 10 ml. Phenyl tetraacetyl-β-D-thioglucoside (1.00 g.) was added and the solution placed in a polarimeter tube. No mutarotation was observed during the course of over two hours. The solution was poured into water and treated as above. There was recovered 0.99 g. (99%) of starting material, m. p. 117–118°; mixed m. p. 117–118°. Thus bromoacetic acid, a constituent which might conceivably arise as a by-product in the cleavage reaction, is in no way responsible for the cleavage.

α-D-Glucose Pentaacetate and Bromine in Methanol.—α-D-Glucose pentaacetate (1.00 g.) was placed in methanol (10 ml.), in which it remained essentially undissolved. Bromine (1.5 ml.) was added to the mixture, causing rapid solution. The solution stood for two hours and was poured into 50 ml. of water. The clear, red solution was decolorized by the addition of sufficient sodium bisulfite, then extracted twice with 30-ml. portions of ether. The aqueous layer was strongly dextro-rotatory (0.34°), while the first ether extract was essentially void of rotation (0.02°), indicating that bromine in methanol had brought about deacetylation of the glucose pentaacetate.

α-D-Glucose Pentaacetate and Bromine in Propionic Acid.—α-D-Glucose pentaacetate (1.00 g.) in propionic acid (20 ml.) was treated with bromine (1.5 ml.) and permitted to stand at room temperature for six hours. The mixture was poured into water (75 ml.), decolorized with sufficient solid sodium bisulfite, extracted with ether, and processed as before. There resulted 1.01 g. of lachrymatory amber sirup as the crude product, $[\alpha]^{25}\text{D}$ 51.4° ($CHCl_3$; *c*, 2.397).

To see if bromine was essential for transacylation, this constituent was omitted from the above mixture. α-D-Glucose pentaacetate (1.00 g.) was dissolved in propionic acid (20 ml.) and the mixture treated as above except that the sodium bisulfite treatment was eliminated. The crude product was a white solid weighing 0.98 g. After one recrystallization from 2-propanol the substance had m. p. 112–112.5° and showed no melting point depression when mixed with starting material.

α-D-Glucose Pentaacetate and Bromine in Acetic Acid.—α-D-Glucose pentaacetate (1.00 g.) was dissolved in acetic acid (20 ml.) and bromine (1.5 ml.) was added. After standing for eighteen hours at room temperature the mixture was poured into water and the product isolated in the usual fashion. The crude product weighed 0.74 g., melted at 110–111.5°, showed no mixed melting point depression (111–112°) with starting material, and had $[\alpha]^{25}\text{D}$ 100.0° ($CHCl_3$; *c*, 4.006).

Summary

On treatment of phenyl, benzyl or ethyl tetraacetyl-β-D-thioglucosides with about thirteen equivalents of bromine in acetic acid, α-D-glucose pentaacetate is formed in good yield. This reaction, involving cleavage of the thiophenyl moiety and replacement with acetoxy, has been shown to be due to bromine alone, and to no other possible constituent of the reaction mixture. In addition, bromine seems capable of labilizing the acetyl functions of several acetylated carbohydrate derivatives, producing deacetylation when methanol is employed as solvent, and transacylation when propionic acid is employed as solvent.

STANFORD UNIVERSITY, CALIFORNIA

RECEIVED OCTOBER 10, 1947