Experimental[9]

α-D-Lyxopyranose Tetrabenzoate (I).—Ten grams of pure α-D-lyxose[10] ($[\alpha]^{20}D$ −13.9° at equilibrium in water) was suspended in 60 ml. of anhydrous pyridine previously cooled to 2° and, with efficient stirring, treated with 48 ml. of benzoyl chloride at such a rate that the temperature of the reaction mixture remained at 0–4°. The slurry was held at 0° for three hours, at 5° overnight and then at 60° for 0.75 hour; after decomposition of the excess benzoyl chloride with crushed ice, the mixture was diluted with methylene dichloride and washed successively with ice-water, cold 3 *N* sulfuric acid and aqueous sodium bicarbonate. After desiccation over sodium sulfate and filtration through a layer of decolorizing carbon, the solution was concentrated *in vacuo* to a stiff sirup. Solution of this latter in 320 ml. of warm absolute ethanol led to the spontaneous separation of stubby prisms (28.3 g., 75%) melting at 137° and rotating −49.4° in chloroform. After two recrystallizations from approximately 12 parts of absolute ethanol the α-D-lyxopyranose tetrabenzoate melted at 138–139°[11] and showed in chloroform a rotation of −49.0° (*c*, 2.16). Further recrystallization failed to change these values.

Anal. Calcd. for $C_{33}H_{26}O_9$: C, 69.96; H, 4.63. Found: C, 69.78; H, 4.70.

Ten grams of α-D-lyxose was dissolved in 80 ml. of anhydrous pyridine (by warming to about 40°), the mixture left at room temperature for 24 hours, treated with 48 ml. of benzoyl chloride and finally worked up as described above, to give crude α-D-lyxopyranose tetrabenzoate in a yield of 62%. Chromatography of the material remaining in the mother liquor gave fractions with levorotations as great as −90.6° but none of these could be induced to crystallize.

(9) Melting points were measured with a calibrated Anschütz-type thermometer completely immersed in the bath liquid. Rotations are specific rotations for the D line of sodium at 20°; concentration is expressed in g. of substance per 100 ml. of solution.

(10) H. G. Fletcher, Jr., H. W. Diehl and C. S. Hudson, THIS JOURNAL, **72**, 4546 (1950).

(11) In the earlier part of this investigation, a crystalline α-D-lyxopyranose tetrabenzoate was obtained which, after repeated crystallization, melted at 111–117°, showed a rotation of −48.9° in chloroform and gave satisfactory analytical values for carbon and hydrogen. Upon solution in warm alcohol and seeding with the higher-melting form obtained later, this low-melting material was converted to the form of m.p. 138–139°; it is therefore probably a dimorphous form of the higher-melting material.

Tribenzoyl-α-D-lyxopyranosyl Bromide (II).—Five grams of crystalline α-D-lyxopyranose tetrabenzoate, prepared as described above, was dissolved in 8 ml. of methylene dichloride and treated with 16 ml. of a solution of hydrogen bromide in glacial acetic acid (*ca.* 32% HBr). Polarimetric observations at 20° showed that the reaction was essentially complete in one-half hour; the reaction mixture was then diluted with methylene dichloride and washed with cold water and cold aqueous sodium bicarbonate. The methylene dichloride solution was dried with sodium sulfate and, after filtration through decolorizing carbon, the solution was concentrated *in vacuo* to a clear, colorless sirup. A sample of this material, dried *in vacuo* at 40°, showed in dry, alcohol-free chloroform a rotation of −58.1° (*c*, 4.84). All attempts to obtain the compound in crystalline form failed.

Reaction of Tribenzoyl-α-D-lyxopyranosyl Bromide with Methanol in the Absence of an Acid Acceptor.—Tribenzoyl-α-D-lyxopyranosyl bromide prepared from 10 g. of α-D-lyxopyranose tetrabenzoate as described above was dissolved in 20 ml. of methylene dichloride and the solution diluted to 200 ml. with absolute methanol. Polarimetric observations at 20° showed that the reaction was essentially complete after one hour. Fourteen milliliters of 1.5 *N* barium methylate was then added and the mixture left at 5° for two days. The pale yellow solution was then deionized by successive passage through columns of Amberlite IR-120[12] and Duolite A-3[13] and, together with the aqueous washings from the columns, concentrated *in vacuo* to a sirup. Solution of this latter in a mixture of methanol and ethyl acetate led to the isolation of 2.32 g. (80%, based on the α-D-lyxopyranose tetrabenzoate used) of crude crystalline material melting at 95–108°. Three recrystallizations from methanol–ethyl acetate gave material rotating in water +58.9° (*c*, 1.91) and melting at 108–109° either alone or in admixture with authentic methyl α-D-lyxopyranoside. Methyl α-D-lyxopyranoside has been reported to have a rotation of +59.4° in water and a melting point of 108–109°.[14]

Acknowledgment.—The authors wish to thank Mrs. Margaret M. Ledyard and Mr. William C. Alford of this Laboratory for combustion analyses.

(12) Product of the Resinous Products and Chemical Co., Washington Square, Philadelphia 5, Pa.

(13) Product of the Chemical Process Co., 901 Spring Street, Redwood City, Calif.

(14) F. P. Phelps and C. S. Hudson, THIS JOURNAL, **48**, 503 (1926).

BETHESDA, MD. RECEIVED FEBRUARY 21, 1951

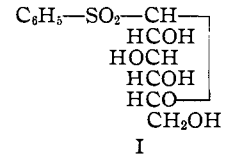
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY]

Periodate Oxidations of Phenyl β-D-Thioglycopyranosides, Phenyl β-D-Glucopyranosyl Sulfones and Related Compounds

BY WILLIAM A. BONNER AND RICHARD W. DRISKO

When phenyl β-D-thioglucopyranoside or its tetraacetate are treated with periodate or iodate solutions, elemental iodine is formed. That this is due to oxidation of the sulfur atom to the sulfone or sulfoxide state has been shown by the fact that the action of periodic acid on ethyl sulfide produces iodine and ethyl sulfone. Periodate ring size determinations on phenyl β-D-glucopyranosyl sulfone and several related compounds were hampered by an ambiguous, fading end-point in the back titrations with iodine. This proved due to the susceptibility of the dialdehyde oxidation products to further oxidation by iodine. When the dialdehydes were removed by extraction prior to analysis for excess periodate, the quantities of periodate consumed and formic acid produced indicated the presence of a pyranose ring in each case.

Methods for the synthesis of alkyl and aryl β-D-glycopyranosyl sulfones, such as I, have recently been reported.[1] In attempts to establish experimentally the ring size in I, it was found that the standard periodate procedures[2] led to haphazard results. Similarly, when phenyl β-D-thioglucopyranoside or its acetate, or phenyl β-D-selenoglucopyranoside reacted with periodate, the reaction again proved anomalous in that elemental iodine was produced.[3] The present paper describes more detailed observations along these lines.



I

When phenyl β-D-thioglucopyranoside was dissolved in *ca.* 0.7 *N* periodic acid and allowed to

(1) W. A. Bonner and R. W. Drisko, THIS JOURNAL, **70**, 2435 (1948).

(2) E. L. Jackson in Chap. 8, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944.

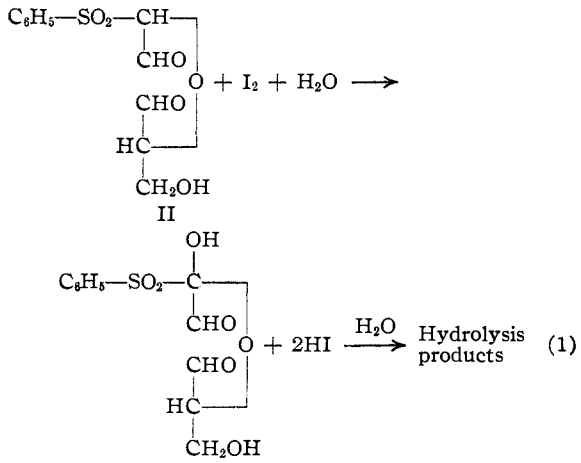
(3) W. A. Bonner and Ann Robinson, THIS JOURNAL, **72**, 354 (1950).

stand at room temperature, the solution slowly precipitated a brown solid. This was identified as iodine by its odor, its coloration with starch solution, its extractability into chloroform, and its reduction by arsenite. When phenyl β-D-thioglucopyranoside was warmed with 10% potassium iodate solution, then acidified, iodine was again liberated. Similar behavior was noted when either periodate or iodate acted on phenyl tetraacetyl-β-D-thioglucopyranoside. The liberation of iodine under these conditions has been reported previously only for phenyl β-D-selenoglucopyranoside.[3] A periodate oxidation establishing the ring size of the ethyl α-D-thioglucoside of Schneider and Sepp[4] as furanoside is recorded[5] with no mention of iodine formation, but in this instance the oxidant was used in only 0.025 *M* concentration.

Since the periodate oxidation of ordinary glycosides produces no iodine, it is reasonable to assign the present liberation of iodine to the oxidation of the sulfur atom of the thioglucoside to the sulfoxide or sulfone state. Such was proved the case by the fact that periodic acid acted on ethyl sulfide to liberate iodine and form ethyl sulfone. Acidified potassium iodate solution also gave iodine in the presence of ethyl sulfide.

Attempts were made to establish the pyranose ring in phenyl β-D-glucopyranosyl sulfone (I) by the usual method[2] involving destruction of the excess periodic acid with arsenite, followed by determination of the excess arsenite by titration with standard iodine solution. These were hampered, however, by the fact that the end-point in the final titration (starch indicator) faded rapidly. Addition of further iodine regenerated the end-point color, which again faded rapidly. This process could be continued until several ml. of *ca.* 0.1 *N* iodine had been added beyond the first end-point appearance, when the color finally persisted and the total iodine volume led to ambiguous results. The same phenomenon was noted with sodium periodate solution.

It seemed reasonable to suppose that the fading end-point resulted by iodine oxidation of the anticipated periodate cleavage product, II, as in Equation (1).



(1)

That such was the case was shown by the following facts. Removal of II by continuous extraction with ethyl acetate *prior to* iodometric determination of the excess periodic acid permitted analysis for the excess in the usual way. The amount of periodic acid consumed by I was in accord with a pyranose ring, as was also the liberation of one mole of formic acid during the oxidation. Similar results with regard to the fading end-point and necessity of extraction were also obtained with phenyl β-D-xylopyranosyl sulfone and ethyl β-D-glucopyranosyl sulfone. Finally, when the sirupy material, II, recovered on evaporation of the ethyl acetate extract was redissolved in water and treated with iodine solution in the presence of starch, immediate discharge of the iodine color resulted.

Since the aldehyde groupings in the periodate cleavage products of ordinary glycosides are not further oxidized under the conditions of the analysis, and since the sulfur atom in II is already fully oxidized, the hydrogen at carbon one must be the center undergoing oxidation. This is reasonable, since it is activated by the adjacency of both a sulfone group and a carbonyl group. The ready oxidation at this position is also in accord with the reducing properties previously reported for I.[1]

Experimental

Periodate and Iodate Oxidations of Phenyl β-D-Thioglucopyranoside.—Phenyl β-D-thioglucopyranoside (0.2010 g.) was dissolved in 0.670 *N* periodic acid (8.03 ml.) and the solution allowed to stand overnight. The following day it contained brown crystals, identified as iodine by the criteria previously noted.

Two samples of phenyl β-D-thioglucopyranoside (0.0996 g. and 0.3800 g.) were each dissolved in 0.4007 *N* periodic acid (25.00 ml.). After standing stoppered at 25° for four hours, the iodine in each mixture was quantitatively extracted into chloroform. The chloroform extracts were quantitatively extracted free of iodine with 40% potassium iodide solution. Titration of the latter extracts with 0.05155 *N* sodium thiosulfate required 2.49 and 10.66 ml., respectively, for the two samples. These correspond to values of 5.10 and 5.68 for the ratio (moles thioglucoside consumed/moles iodine produced), values intermediate between the ratios 3.50 for oxidation to the sulfone and 7.00 for oxidation to the sulfoxide. Thus either oxidation was incomplete or, equally probably, some of the iodine produced was consumed in reaction with the periodate cleavage product, II, formed simultaneously. The method for iodine assay based on the above double extraction was tested independently on a known weight of iodine and found adequate. 1.134 meq. of iodine weighed out, extracted and analyzed as above showed up as 1.118 meq.

Phenyl β-D-thioglucopyranoside (0.2080 g.) was dissolved in 10% aqueous potassium iodate (25 ml.). The solution was warmed for 15 minutes with no apparent reaction. Cautious acidification, however, caused immediate liberation of iodine.

Similar observations were noted with phenyl tetraacetyl-β-D-thioglucopyranoside.

Ethyl Sulfone.—Ethyl sulfide (2.5 ml.) was dissolved in a mixture of methanol (25 ml.) and 1.4 *N* periodic acid (40 ml.). Iodine was liberated immediately. The mixture was warmed to 60° for five minutes, cooled, and the solid iodine filtered. The iodine in solution was destroyed by addition of saturated aqueous sodium thiosulfate, the mixture filtered, and the filtrate extracted five times with benzene (40-ml. portions). The extract was dried (anhydrous sodium sulfate), filtered, and the solvent removed, leaving 0.40 g. of light tan solid, m.p. 67–70°. This was purified by leaching with carbon disulfide, which left a white solid, m.p. 73–74°. The latter showed no mixed m.p. depression with authentic ethyl sulfone, m.p. 72–73°, obtained by the hydrogen peroxide oxidation of ethyl sulfide.[6]

(4) W. Schneider and Johanna Sepp, *Ber.*, **49**, 2054 (1916).

(5) M. L. Wolfrom, S. W. Waisbrot, D. I. Weisblat and Alva Thompson, THIS JOURNAL, **66**, 2063 (1944).

(6) R. Pummerer, *Ber.*, **43**, 1407 (1910).

Periodate Oxidations of Alkyl and Aryl β-D-Glycopyranosyl Sulfones.—When phenyl β-D-glucopyranosyl sulfone or phenyl β-D-xylopyranosyl sulfone were oxidized with periodic acid or sodium periodate solutions, and the excess oxidant determined in the usual way,[2] a rapidly fading endpoint in the final iodine titration made the analytical figures meaningless. The difficulty was circumvented as follows.

Phenyl β-D-glucopyranosyl sulfone hydrate[1] (0.1695 g.) was dissolved in 0.487 *N* sodium periodate (5.00 ml.) and diluted with distilled water (20 ml.). After standing at room temperature overnight the solution was extracted continuously with ethyl acetate for eight hours. The aqueous layer was transferred quantitatively to a flask, treated with excess sodium bicarbonate, and diluted with 0.0502 *N* sodium arsenite (5.00 ml.) and 20% potassium iodide (1 ml.). After ten minutes the solution was titrated with 0.50 ml. of 0.0500 *N* iodine. Moles $NaIO_4$/moles sulfone: calcd. 2.00; found, 2.09.

When this method was applied to other sulfones the following results were obtained. Moles $NaIO_4$/moles sulfone: calcd. 2.00; found for ethyl β-D-glucopyranosyl sulfone, 1.80; found for phenyl β-D-xylopyranosyl sulfone, 2.16.

Phenyl β-D-glucopyranosyl sulfone hydrate (0.1000 g.) was dissolved in 0.4630 *N* sodium periodate (3.00 ml.) and allowed to stand overnight. The solution was diluted with water (250 ml.) and titrated potentiometrically with 0.0992 *N* sodium hydroxide (3.10 ml.) to *p*H 7.00. Moles HCOOH/moles sulfone: calcd. 1.00; found, 0.99.

STANFORD, CALIF. RECEIVED FEBRUARY 12, 1951

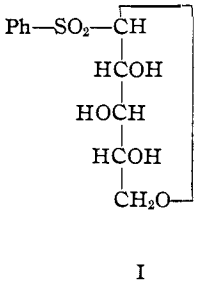
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

The Action of Phenylhydrazine on the Periodate Degradation Products of Phenyl β-D-Glycopyranosyl Sulfones

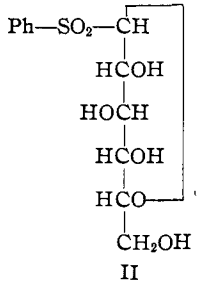
BY WILLIAM A. BONNER AND RICHARD W. DRISKO

When the dialdehyde sirups obtained by action of periodic acid on phenyl β-D-xylopyranosyl or β-D-glucopyranosyl sulfones react with phenylhydrazine, cleavage occurs. Benzenesulfonic acid and glyoxal phenylosazone have been identified among the cleavage products. A mechanism is postulated wherein phenylhydrazine oxidizes the α-hydrogen atom in the dialdehyde sirups to produce an unstable hemiacetal, which then decomposes hydrolytically to the products. Phenylhydrazine reacts with phenyl β-D-glycopyranosyl sulfones themselves to produce the corresponding D-glycosazone. A similar mechanism involving phenylhydrazine as oxidant rationalizes the observed facts.

Phenyl β-D-xylopyranosyl sulfone (I) and phenyl β-D-glucopyranosyl sulfone[1] (II) have recently been subjected to periodate ring size determinations.[2] The results were anomalous in that the periodate

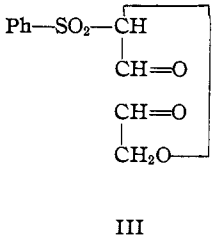


I

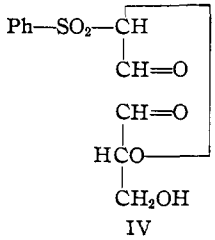


II

degradation products, III and IV, respectively, were oxidized during the final back-titration with iodine.[3] Only on extraction of III or IV prior to the standard analytical procedure[3] were the rings in



III



IV

I and II shown to be pyranoid. The oxidation products III and IV proved to be sirups which could not be crystallized, though analysis of IV gave reasonably acceptable results. In an effort to characterize III and IV more fully we have attempted their reaction with phenylhydrazine, wherein unexpected results were again encountered.

When III reacted with phenylhydrazine a sulfur-free product was obtained which proved to be the phenylosazone of glyoxal. Similar results were noted with *p*-bromophenylhydrazine. The action of phenylhydrazine or *p*-bromophenylhydrazine on IV likewise gave the corresponding osazone derivative of glyoxal. These facts, coupled with the loss of optical activity during the reactions, indicated that cleavage of III and IV occurred by action of the phenylhydrazine, and the other cleavage products, postulated as benzenesulfonic acid and (from IV) D-glyceraldehyde, were accordingly sought.

From the cleavage products of IV benzenesulfonic acid was isolated and characterized as its S-benzylthiuronium salt. In another experiment the benzenesulfonic acid from IV was characterized by comparison of the infrared spectrum of its sodium salt with an authentic sample of sodium benzenesulfonate (Fig. 1).

Although we have isolated a sulfur-free, reducing sirup after removal of glyoxal phenylosazone on the phenylhydrazine cleavage of IV, we have been unable to characterize this as glyceraldehyde through the osazone. This is perhaps not surprising in view of our difficulties in forming crystalline glyceraldehyde phenylosazone from an authentic sample of D-glyceraldehyde.

The simplest interpretation of the cleavage of III and IV with phenylhydrazine is the following, wherein phenylhydrazine acts as an oxidant in one of the stages of reaction.

The intermediate oxidation product, V, being a hemiacetal, might be expected to decompose spontaneously producing glycolaldehyde or glyceraldehyde, VI, and the intermediate VII. Hydrolysis of VII in the manner shown would then lead to the observed products.

(1) W. A. Bonner and R. W. Drisko, THIS JOURNAL, **70**, 2435 (1948).

(2) W. A. Bonner and R. W. Drisko, *ibid.*, **73**, 3699 (1951).

(3) E. L. Jackson in Chap. 8, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944.