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.

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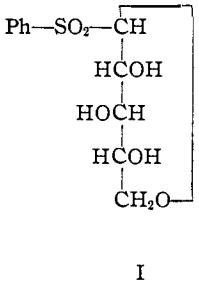
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

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

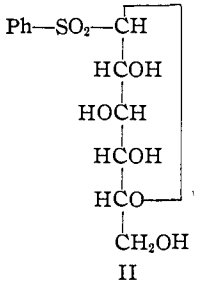
BY WILLIAM A. BONNER AND RICHARD W. DRISKO

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

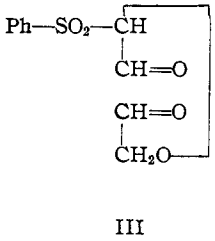


I

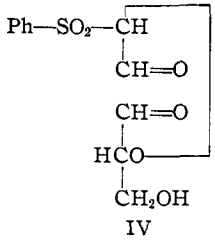


II

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.

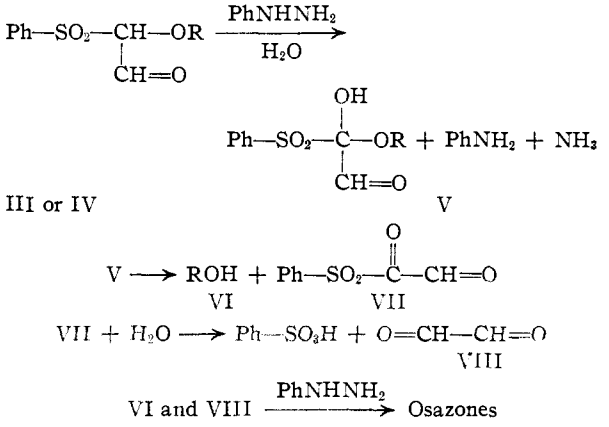
The simplest interpretation of the cleavage of III and IV with phenylhydrazine is the following, wherein phenylhydrazine acts as an oxidant in one of the stages of reaction.

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).

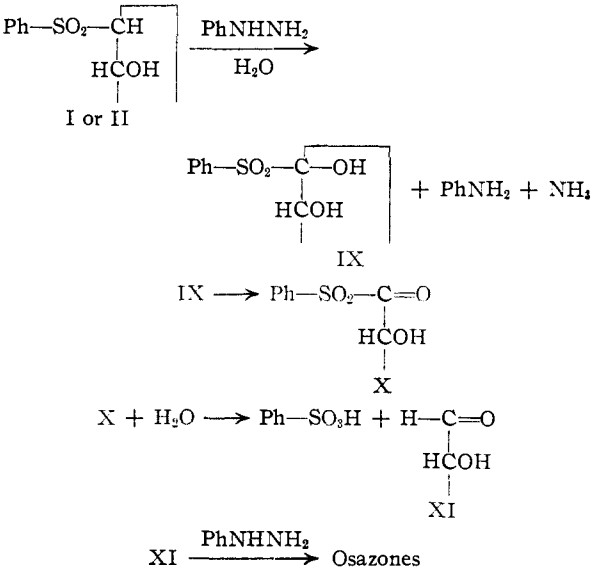
(2) W. A. Bonner and R. W. Drisko, *ibid.*, **73**, 3699 (1951).

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



While the formation of osazones from aldoses is no longer believed to occur with phenylhydrazine acting as an oxidant,[4] but rather to proceed *via* the Amadori rearrangement,[5] it is difficult to see how the latter mechanism could operate in the present case. The ease of oxidation of III and IV with iodine has already been pointed out,[2] and its seems probable that the activating effect of the sulfone and carbonyl groups in III and IV permit a similar oxidation here with phenylhydrazine. That III and IV do not initially contain the hydroxyl group postulated in V is shown by the fact that only two moles of periodate were consumed in their production from I and II.[2]

tion of osazones from I and II might be rationalized as



The similarities of the two proposed reaction schemes should be emphasized. The osazones from III and IV are produced much more rapidly than those from I and II, a probable consequence of the added activation by the carbonyl group in III and IV. Clearly, however, the sulfone group in I and II is sufficiently activating to permit cleavage of an apparently comparable type, and the postulation of an oxidative step in the process is supported by the strong reducing properties of I and II.[1] In contrast, phenyl β-D-thioglucopyranoside is non-reducing, and yields no D-glucosazone on treatment with phenylhydrazine.

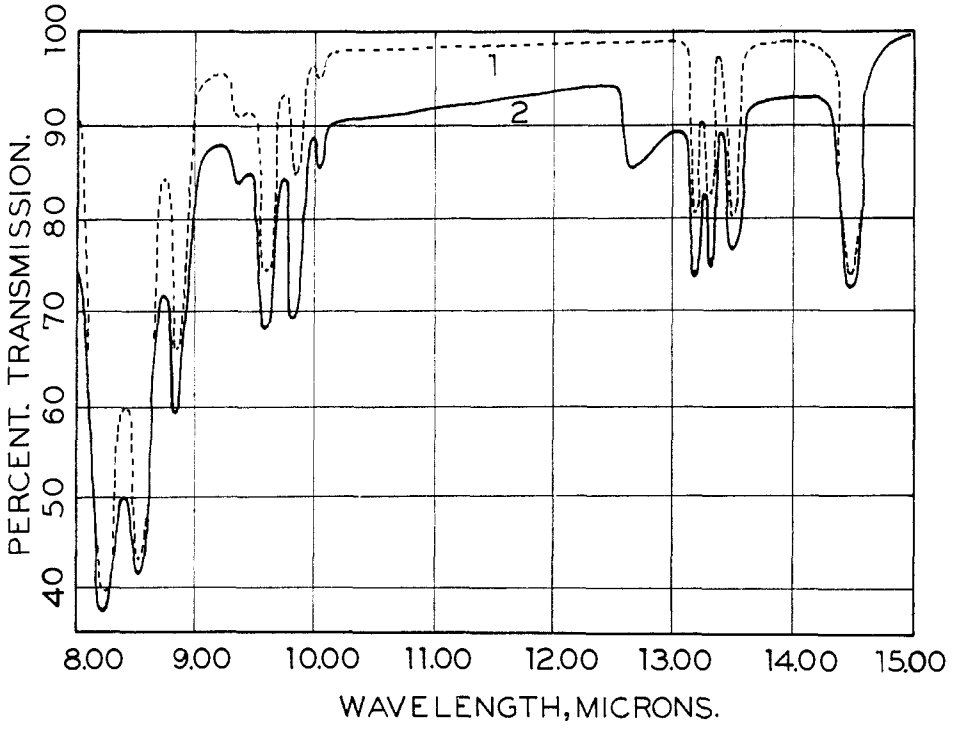


Fig. 1.

The oxidation step above is made more plausible by the fact that I and II themselves produced, respectively, D-xylosazone and D-glucosazone on treatment with phenylhydrazine. Here oxidation would seem an essential initial step, and the produc-

(4) E. Fischer, *Ber.*, **20**, 281 (1887).
(5) F. Weygand, *ibid.*, **73**, 1284 (1940).

Experimental

Phenyl β-D-Glucopyranosyl Sulfone and Sodium Periodate.—Phenyl β-D-glucopyranosyl sulfone hydrate (1.91 g.) was dissolved in 0.487 *N* sodium periodate solution (63 ml.), the mixture allowed to stand at 25° for one hour, and then treated with a hot, saturated solution of strontium hydroxide until faintly pink to phenolphthalein. The precipitated strontium salts were filtered (Celite), and the filtrate extracted continuously with ether for ten hours. The extract was dried, filtered, and evaporated, leaving 1.52 g. (95%) of clear sirup, $[\alpha]^{26}D$ −20.1° (*c* 1.08, ethanol), which reduced Fehling solution instantly. A similar sample (0.5 g.) was redissolved in absolute ethanol, filtered through Norit, and evaporated to dryness at 40° *in vacuo* in a 50-ml. beaker. The film of sirup was dried *in vacuo* over phosphoric anhydride prior to analysis.

Anal. Calcd. for $C_{11}H_{12}O_6S$: C, 48.51; H, 4.44; S, 11.76. Two samples prepared as above had 4.23% and 4.38% ash. When corrected for ash the samples had C, 48.49, 48.68; H, 5.02, 5.12; S, 10.78, 10.86.

Reaction with Phenylhydrazines.—A sample of the above sirupy product was dissolved in hot water and treated with excess phenylhydrazine and sufficient acetic acid to effect solution. On cooling, the phenylosazone crystallized as a yellow solid, m.p. 160–164°. Three recrystallizations from dilute alcohol gave a sample of m.p. 168–170°, alone or admixed with authentic glyoxal phenylosazone.

Anal. Calcd for $C_{14}H_{14}N_4$: C, 70.56; H, 5.90; N, 23.52. Found: C, 70.39, 70.48; H, 5.98, 5.91; N, 23.57, 23.49.

Another sample of the sirup was caused to react with *p*-bromophenylhydrazine as above. The product had m.p. 227–229° after several recrystallizations, and showed no mixed m.p. depression with an authentic sample of glyoxal *p*-bromophenylosazone of m.p. 228–230°.

Phenyl β-D-Xylopyranosyl Sulfone and Sodium Periodate.—Phenyl β-D-xylopyranosyl sulfone (0.88 g.) was oxidized with 0.487 *N* sodium periodate (29 ml.), and the product isolated as before. There resulted 0.70 g. (90%) of colorless, optically inactive sirup.

A portion of this sirup reacted with phenylhydrazine as above to give again glyoxal phenylosazone, m.p. 167.5–169°, mixed m.p. with an authentic sample, 165.5–167.5°.

Another portion of the sirup gave glyoxal *p*-bromophenylosazone with *p*-bromophenylhydrazine. After several recrystallizations the product had m.p. 227–229°, alone or admixed with an authentic sample.

Anal. Calcd. for $C_{14}H_{12}N_4Br_2$: C, 42.42; H, 3.05; N, 14.15. Found: C, 42.93; H, 3.17; N, 13.94.

Benzenesulfonic Acid.—A wide variety of techniques was employed in attempts to isolate benzenesulfonic acid and D-glyceraldehyde after cleavage of IV. The following, with variations, was typical.

Phenyl β-D-glucopyranosyl sulfone hydrate (8.1 g.) was dissolved in hot water (200 ml.) containing sodium metaperiodate (10.8 g.). After three days the mixture was saturated with sodium sulfate and extracted continuously with ether for three days. The extract was dried and concentrated to give 2.9 g. of the sirup IV.

A portion (2.0 g.) of the sirup was dissolved in water (150 ml.) and the mixture treated with phenylhydrazine (2.3 ml.) and sufficient acetic acid to effect solution. After 30 minutes on the steam-bath the glyoxal phenylosazone was removed by fifteen extractions with 20-ml. portions of ether.

The aqueous residue was made alkaline to *p*H 12 and extracted several times with ether to remove excess phenylhydrazine. It was then neutralized with cond. hydrochloric acid and evaporated to dryness at 100° *in vacuo*, yielding 1.8 g. of tan solid. This was leached with six 20-ml. portions of warm absolute ethanol, 0.9 g. remaining undissolved. The solution was evaporated, and the residue leached with 2-propanol. The undissolved residue readily gave an S-benzylthiuronium salt, m.p. 148° alone or admixed with authentic S-benzylthiuronium benzenesulfonate. Later samples so obtained melted and analyzed correctly but, unaccountably, showed a m.p. depression when mixed with an authentic sample.

Anal. Calcd. for $C_{14}H_{16}O_3N_2S_2$: C, 51.83; H, 4.93; N, 8.64; S, 19.77. Found: C, 51.66; H, 5.08; N, 8.58; S, 19.71.

A portion of the original sirup (0.9 g.) was treated with phenylhydrazine (0.7 ml.) as before, and the glyoxal phenylosazone removed by ether extraction. The aqueous residue was made alkaline, then acidic, extracting with ether each time. Neutralization and evaporation gave a tan residue which was again leached with absolute ethanol. The leachings were filtered through Norit and evaporated giving 0.05 g. of fluffy solid. This showed an identical infrared spectrum (Fig. 1) with authentic sodium benzenesulfonate when measured in mineral oil suspension on a Perkin–Elmer Infrared Spectrophotometer. The single discrepancy in the spectra may be due to an impurity or a momentary failure in the instrument. We are indebted to Prof. John H. Wise for the spectral measurements.

In another experiment where the glyoxal phenylosazone was filtered, a solid slowly precipitated in the filtrate, m.p. 131–134°. After three recrystallizations from dilute 2-propanol the m.p. was constant at 135.5–136.5°, and the sample analyzed correctly for the phenylhydrazide of benzenesulfonic acid.

Anal. Calcd. for $C_{12}H_{12}O_2N_2S$: C, 58.04; H, 4.87; N, 11.28; S, 12.91. Found: C, 58.11, 58.12; H, 4.88, 4.74; N, 11.28; S, 13.09, 13.11.

This substance appears to show polymorphism, as its melting point in the literature[6] varies from 145 to 164.5°.

Phenylhydrazine and Phenyl β-D-Glycopyranosyl Sulfones.—Phenyl β-D-glucopyranosyl sulfone hydrate (0.3 g.) was dissolved in water (20 ml.) and the solution treated with phenylhydrazine (1 ml.) and enough acetic acid to effect homogeneity. After a three-hour period on the steam-bath the mixture was cooled and the osazone, 13 mg., which precipitated on standing filtered, m.p. 183–185°. Recrystallization from dilute 2-propanol raised the m.p. to 195–196°. A mixed m.p. with authentic D-glucosazone, m.p. 197–198°, showed no depression.

Phenyl β-D-xylopyranosyl sulfone (0.3 g.) was treated similarly. After 90 minutes at 100°, 0.53 mg. of osazone, m.p. 150–152°, was filtered. One recrystallization gave a sample, m.p. 151–152°, showing no depression when mixed with authentic D-xylosazone, m.p. 155°.

When phenyl β-D-thioglucopyranoside was similarly treated, no evidence of osazone formation was noted after five hours on the steam-bath.

STANFORD, CALIFORNIA RECEIVED MARCH 19, 1951

(6) Beilstein, "Handbuch der organischen Chemie," Vol. 15, p. 413.