in 12 cc. of 66% alcohol and heated to boiling in the presence of 325 micromoles of paraperiodic acid in 0.5 cc. of water. The red solutions were permitted to stand for one hour, and the unused periodic acid as well as the sum of iodic and periodic acids were determined as described before. In these determinations 3.07 and 2.96 moles of periodic acid were consumed by one mole of glucosazone; but the values found in two experiments for the total oxidizing capacity showed that 4.1 gram-atoms of oxygen had been used.

Oxidation of the 1,2-bis-Phenylhydrazone of Mesoxalaldehyde (III).—When 940 mg. of III was boiled for five minutes with 200 cc. of 50% ethanol containing 1.85 g. of iodic acid, a dark red-brown solution resulted which on being cooled deposited 310 mg. of the crude oxidation product (yield 33%). This material was purified by precipitation with acid from its solution in hot 0.2 *M* sodium carbonate and then by three recrystallizations from ethanol. The *pyrazolone* I was obtained as small orange needles melting at 150°, soluble in alkali, slightly soluble in alcohol and chloroform, insoluble in water and acid.

In another experiment, 1.85 g. of silver nitrate in 200 cc. of water were added to a suspension of 1.33 g. of the aldehyde III in 150 cc. of ethanol. To this mixture 16.5 cc. of *N* potassium hydroxide was added dropwise with constant stirring in the course of one hour.[12] An undissolved fraction, from which a large proportion of the unchanged aldehyde III could be recovered, was filtered off and the filtrate acidified when 160 mg. of the crude *pyrazolone* I separated. Three recrystallizations from alcohol and chloroform brought the melting point to 149–150°.

For purposes of comparison 1-phenyl-4-phenylhydrazonopyrazolone-5 (I) also was prepared according to Knorr[3] by treating the 1,2-bisphenylhydrazone of mesoxalic acid semialdehyde (II) with acetic anhydride. The starting material had been prepared by Dr. D. B. Sprinson from hydroxypyruvic acid by the method recently published from this Laboratory.[13] The pyrazolone melted at 149–150° and showed no depression of the melting point when mixed with preparations obtained by the oxidation of the aldehyde III.

Absorption Spectra.—The spectra of compounds I, II and III, reproduced in Fig. 1, were determined with a Beckman photoelectric quartz spectrophotometer. About 0.023 millimolar solutions in absolute ethyl alcohol were employed. We are indebted to Dr. E. Brand and Miss M. Crymble of this Department for help with these measurements.

Acknowledgments.—The authors wish to thank Mr. W. Saschek for the microanalyses.

Summary

Glucose phenylosazone, oxidized at room temperature with periodic acid, gave rise to the expected aldehyde, the 1,2-bis-phenylhydrazone of mesoxalaldehyde (III) which was further characterized by conversion to its semicarbazone (IV) and the corresponding tris-phenylhydrazone (V).

At elevated temperatures the aldehyde III was further oxidized by the iodic acid present to 1-phenyl-4-phenylhydrazonopyrazolone-5 (I) which can also be produced by the action of dehydrating agents on the 1,2-bis-phenylhydrazone of mesoxalic acid semialdehyde (II). The probable mechanism of these transformations is discussed briefly.

(12) M. Delépine and P. Bonnet, *Compt. rend. acad. sci.*, **149**, 39 (1909).

(13) D. B. Sprinson and E. Chargaff, *J. Biol. Chem.*, **164**, 417 (1946).

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[CONTRIBUTION FROM THE CHEMISTRY LABORATORY, NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Action of Copper Sulfate on the Phenylosazones of the Sugars. V. The Phenylosotriazoles of L-Rhamnose, L-Fucose and Melibiose

BY W. T. HASKINS, RAYMOND M. HANN AND C. S. HUDSON

This paper is a continuation of the articles previously published[1] describing the conversion of the sugar phenylosazones to the corresponding phenylosotriazoles through the action of copper sulfate. The phenylosotriazole from L-rhamnose (6-desoxy-L-*arabo*-hexose phenylosotriazole) is only moderately soluble in water at ordinary temperature and crystallizes readily from concentrated aqueous solutions, while the phenylosotriazoles from L-fucose and melibiose (6-desoxy-L-*lyxo*-hexose phenylosotriazole and 6-α-D-galactopyranosyl-D-*arabo*-hexose phenylosotriazole) are very soluble in water and crystallize best from non-aqueous solvents. All three phenylosotriazoles have sharp melting points and solutions of them do not mutarotate, in common with the properties of the other sugar phenylosotriazoles that were described in the previous articles.

The structures of the L-rhamnose and L-fucose phenylosotriazoles were proven to be those shown in the formulas by oxidation with sodium metaperiodate which in each case gave high yields of 2-phenyl-4-formyl-2,1,3-triazole together with the appropriate amounts of formic acid and acetaldehyde. The structure of melibiose phenylosotriazole was demonstrated by hydrolysis with dilute hydrochloric acid to produce D-glucose phenylosotriazole (D-*arabo*-hexose phenylosotriazole) and D-galactose in good yields.

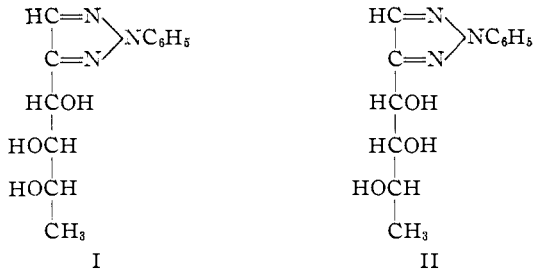
We are indebted to Mr. Charles A. Kinser and Mrs. Betty Mount for the microchemical analyses.

Experimental

L-Rhamnose Phenylosotriazole.—To a suspension of 10 g. of L-rhamnose phenylosazone[2] in 900 ml. of boiling water was added a solution of 8.0 g. (1.1 molecular equivalents) of copper sulfate pentahydrate in 100 ml. of boiling water and the mixture was refluxed one hour. The cooled solution was filtered and on concentrating it *in vacuo* to 100 ml., spontaneous crystallization of the product took place; the crystals were dissolved by warming the mixture

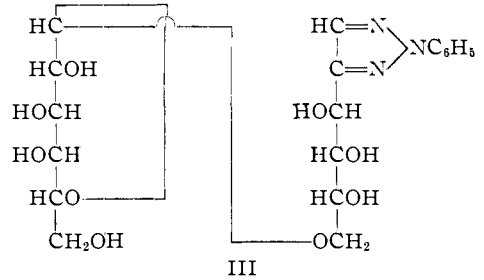
(1) Number IV was published in THIS JOURNAL, **69**, 1050 (1947).

(2) Fischer and Zach, *Ber.*, **45**, 3770 (1912).



I
L-Rhamnose phenylosotriazole

II
L-Fucose phenylosotriazole



III
Melibiose phenylosotriazole

and the solution was filtered through a thin layer of decolorizing carbon. The osotriazole crystallized from the filtrate on cooling as clusters of needles; the yield was 4.0 g. and an additional 1.4 g. was obtained by concentration of the mother liquor to 50 ml., making the total yield 5.4 g. (74%). The material was recrystallized from 20 parts of water or from 75 parts of U. S. P. chloroform, and when pure it melted at 136–137°[3] and rotated +101.5° in pyridine solution (*c*, 0.84) and +49.4° in aqueous solution (*c*, 0.41). It is very soluble in methyl and ethyl alcohols, acetone and warm water, moderately soluble in boiling chloroform and sparingly soluble in ether, petroleum ether, cold water and cold chloroform.

Anal. Calcd. for $C_{12}H_{15}N_3O_3$: C, 57.82; H, 6.07. Found: C, 57.78; H, 5.80.

L-Rhamnose Phenylosotriazole Tribenzoate.—The benzoylation of L-rhamnose phenylosotriazole in pyridine solution with benzoyl chloride gave a quantitative yield of the tribenzoate which upon recrystallization from 10 parts of alcohol formed clusters of prismatic needles melting at 101–102° and rotating +35.3° in chloroform (*c*, 0.89). It is soluble in pyridine, acetone, ether and warm alcohol and nearly insoluble in water, hexane and cold alcohol.

Anal. Calcd. for $C_{33}H_{27}N_3O_6$: C, 70.58; H, 4.85; C_6H_5CO, 56.2. Found: C, 70.77; H, 4.84; C_6H_5CO, 56.0.

L-Fucose Phenylosotriazole.—The phenylosotriazole of L-fucose was prepared from 10 g. of L-fucose phenylosazone[4] by the same method. Due to its relatively high solubility in water, it was necessary to remove the excess copper from the reaction mixture as the sulfide, neutralize the copper-free filtrate with 10 g. of barium carbonate and concentrate the filtered solution to a sirup which was dried by three successive concentrations with 25 ml. of absolute alcohol; the dry sirup was dissolved in 25 ml. of chloroform and diluted with 25 ml. of hexane to form a sirupy phase which gradually crystallized while standing at 5°. The yield was 6.8 g. of dark colored crystals which were recrystallized, first from 10 parts of benzene and then from 10 parts of water, to give 4.8 g. (66%) of colorless needles melting at 83–84° and rotating +20.0° in aqueous solution (*c*, 0.86). The compound is soluble in alcohol, pyridine, acetone, chloroform, ether, glacial acetic acid and water at room temperature, sparingly soluble in ice water and nearly insoluble in cold benzene and hexane.

Anal. Calcd. for $C_{12}H_{15}N_3O_3$: C, 57.82; H, 6.07. Found: C, 58.03; H, 6.28.

L-Fucose Phenylosotriazole Triacetate.—The acetylation of 1.0 g. of L-fucose phenylosotriazole with acetic anhydride (8 ml.) and fused sodium acetate (0.25 g.) by warming on the steam-bath for two hours followed by the addition of ice water, produced a quantitative yield (1.5 g.) of the triacetate. It was recrystallized from 5 parts of alcohol, forming needles which melted at 88–89° and rotated +44.1° in chloroform (*c*, 0.81). It is soluble in acetone, ether, pyridine and warm alcohol and sparingly soluble in water and petroleum ether.

Anal. Calcd. for $C_{18}H_{21}N_3O_6$: C, 57.59; H, 5.64; CH_3CO, 34.4. Found: C, 57.80; H, 5.67; CH_3CO, 34.5.

L-Fucose Phenylosotriazole Tribenzoate.—The benzoylation of L-fucose phenylosotriazole in the usual way with benzoyl chloride and pyridine gave a quantitative yield of the tribenzoyl derivative which, following recrystallization from 10 parts of methyl alcohol, formed elongated prisms melting at 97–98° and rotating −12.0° in chloroform (*c*, 0.86). It is soluble in ether, acetone, warm methyl and ethyl alcohols and chloroform and nearly insoluble in water and hexane.

Anal. Calcd. for $C_{33}H_{27}N_3O_6$: C, 70.58; H, 4.85; C_6H_5CO, 56.2. Found: C, 70.61; H, 4.99; C_6H_5CO, 56.0.

Melibiose Phenylosotriazole.—This was prepared by treating 10 g. of melibiose phenylosazone[5] with 5.3 g. (1.1 molecular equivalents) of copper sulfate pentahydrate by the same procedure employed in the case of L-fucose phenylosotriazole. The sirup from the concentration of the neutralized copper-free reaction mixture was dried by concentration with three 25-ml. portions of absolute alcohol, dissolved in 25 ml. of warm alcohol and, following filtration, diluted with 30 ml. of ether to produce a sirupy phase which crystallized readily upon scratching. The yield was 6.1 g. (74%) of tan colored material which was recrystallized from 25 parts of absolute alcohol; it formed tufts of fine colorless needles melting at 153–154° and rotating +61.2° in aqueous solution (*c*, 0.80). It is very soluble in water, pyridine and warm alcohol and sparingly soluble in ether, acetone, ethyl acetate and cold alcohol.

Anal. Calcd. for $C_{15}H_{25}N_3O_9$: C, 50.58; H, 5.90. Found: C, 50.51; H, 6.10.

The melibiose phenylosotriazole, upon refluxing in 0.5 *N* hydrochloric acid solution for six hours, gave a 92% yield of D-glucose phenylosotriazole (m. p. 195–196°; $[\alpha]^{20}D$ −81.5° in pyridine). A 60% yield of D-galactose ($[\alpha]^{20}D$ +80.0° (equilibrium value in water)), was obtained from the neutralized aqueous filtrate by evaporation to dryness and the addition of a few ml. of glacial acetic acid; these results prove that the structure of the phenylosotriazole is as indicated in formula III.

Sodium Metaperiodate Oxidation of L-Rhamnose and L-Fucose Phenylosotriazoles.—To 0.4000-g. samples of L-fucose and L-rhamnose phenylosotriazoles dissolved in 15-ml. portions of water was added in each case 2.5 molecular equivalents of 0.534 *M* sodium metaperiodate solution; oxidation was rapid and a crystalline precipitate of 2-phenyl-4-formyl-2,1,3-triazole formed in a short time. After standing at 20° for two hours the mixtures were cooled to 5° for two hours and the crystals recovered by filtration and washed with ice water. The yield in each case was nearly quantitative and the product melted at 68–69° and showed no depression of that value when mixed with authentic 2-phenyl-4-formyl-2,1,3-triazole. The mother liquors and washings were diluted to 50 ml.

(3) The melting points were made with the stem of the thermometer fully immersed in the heated bath. The rotations refer to specific rotations $[\alpha]^{20}D$; *c* is the concentration in grams per 100 ml. of solution; the tube length was 4 dm. All of the crystalline compounds were recrystallized to constant melting point and specific rotation.

(4) Votoček, *ibid.*, **37**, 3859 (1904).

(5) Helferich and Rauch, *ibid.*, **59**, 2655 (1926).

and analyzed for consumed periodate, formic acid and acetaldehyde. The results showed that the oxidations were represented within close limits by the equation $C_{12}H_{15}N_3O_3 + 2NaIO_4 \rightarrow C_9H_7N_3O + HCOOH + CH_3CHO + 2NaIO_3 + H_2O$, which proves that the structures of the L-rhamnose and L-fucose phenylosotriazoles are as represented by formulas I and II.

Summary

The phenylosotriazoles of L-rhamnose, L-fucose and melibiose and some of their acetyl and benzoyl derivatives are described.

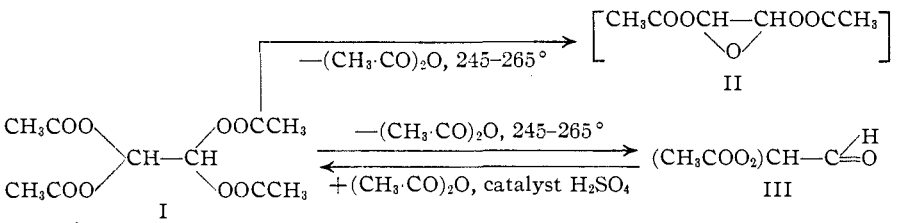
BETHESDA, MARYLAND RECEIVED MARCH 6, 1947

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BANTING INSTITUTE, UNIVERSITY OF TORONTO]

Glyoxal Semiacetate

BY ERICH BAER AND HERMANN O. L. FISCHER

In the course of a study of the pyrolysis of glyoxal tetraacetate (I) in the temperature range of 245–265° (normal pressure) it was observed that the *pure* compound decomposes smoothly, giving rise to volatile liquid reaction products and a small residue of carbonized matter. Fractional vacuum distillation of the slightly colored distillate led to its separation into two major fractions with greatly differing boiling ranges. The main compound (A) of the lower boiling fraction [b. p. (6 mm.) 37–41°] was easily identified as acetic anhydride by its odor, boiling point and its ability to form acetanilide (m. p. 114.5–115.5°). The higher boiling fraction, on repeated fractional distillation *in vacuo* yielded an as yet unknown substance [compound B, b. p. (6 mm.) 92–93°] to which, on the basis of its elementary composition (C, 44.93; H, 4.98) and molecular weight (161.8, cryoscopic in benzene) the empirical formula of $C_6H_8O_5$ was assigned. The presence of two acetyl groups in the molecule and the quantitative formation of glyoxal osazone, together with the fact that the other main product of the pyrolysis is acetic anhydride, made it probable that compound B was either the 1,2-diacetyl 1,2-anhydroglyoxal dihydrate (II) or the 1,1-diacetylglyoxal monohydrate (III).



(IV) $(CH_3COO)_2CH—CH=N—NHC_6H_3(NO_2)_2$-2,4

(V) $(CH_3COO)_2CH—CH=C_{16}H_{22}O_4$

The presence of a free carbonyl group in compound B seemed to be established when a 2,4-dinitrophenylhydrazone IV (m. p. 143–144°) and a dimedone compound V (m. p. 169.5–170.0°) were obtained. It was recognized, however, that the formation of these two unsymmetrically substituted glyoxal derivatives did not prove unequivocally the aldehyde structure of compound B; the possibility of a structural rearrangement (II→III) during the preparation of the hydrazone and the dimedone compound could not be overlooked. It was therefore desirable to obtain an independent proof of the aldehyde structure under conditions which would not occasion rearrangement. Dr. R. N. Jones of Queen's University, Kingston, Ontario,[1] kindly consented to determine the ultraviolet absorption spectrum of compound B and summarized his results as follows: "The substance has a well defined absorption maximum at 2960 Å. (see Fig. 1) with a molecular extinction coefficient of about 10. This is in the correct position and of the correct order of intensity for a saturated aliphatic aldehyde with heavy substituents on the β-carbon atom. The results are reconcilable with the aldehyde structure (III) but not with the alternative oxide ring structure (II)." Thus the absorption spectrum of the compound and the chemical evidence previously cited led to the assignment of structure III to compound B.

With regard to the formation of glyoxal semiacetate we are unable at present to say by which mechanism (I→III or I→II→III) the reaction takes place. The fact that at higher temperatures and in the presence of catalysts the acetates of aldehydes are known[2] to break down with the formation of the aldehyde and acetic anhydride would seem to speak in favor of the direct formation of glyoxal semiacetate (I→III) from glyoxal tetraacetate.

In its structure the glyoxal semiacetate resembles glyoxal semiacetal[3] but is less stable and apparently more inclined to undergo polymerization. In spite of these limitations the glyoxal semiacetate should prove itself a valuable material for synthetic purposes.

(1) Present address: National Research Council, Ottawa, Canada.

(2) J. Houben, "Die Methoden der organischen Chemie," vol. II, 3rd ed., 1925, p. 547.

(3) H. O. L. Fischer and E. Baer, *Helv. Chim. Acta*, **18**, 514 (1935).