Foundation for generous gifts of thymine and D-ribose. The authors also wish to express their appreciation to Mr. Jack Fox for technical assistance.

Summary

The synthesis of 1-D-ribosyl-, 1-D-arabinosyl-, 1-L-arabinosyl-, 1-D-glucosyl- and 1-D-galactosylthymine nucleosides are described. These nucleosides were prepared by reactions between 2,4-diethoxy-5-methylpyrimidine and the proper acetobromo sugar.

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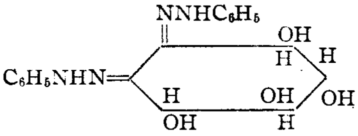
[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY]

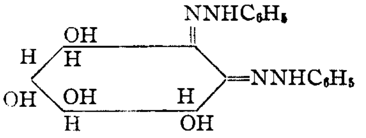
The Action of Periodic Acid on a Cyclohexose Osazone[1]

BY BORIS MAGASANIK[2] AND ERWIN CHARGAFF

It has been shown in a preceding communication[3] that the cyclohexose osazones isolated following the oxidation of *l*- and *d*-inositol by *Acetobacter suboxydans* each consumed three moles of periodic acid per mole of substance. Structure Ia represents the osazone derived from *l*-inositol, Ib that from *d*-inositol.[4]



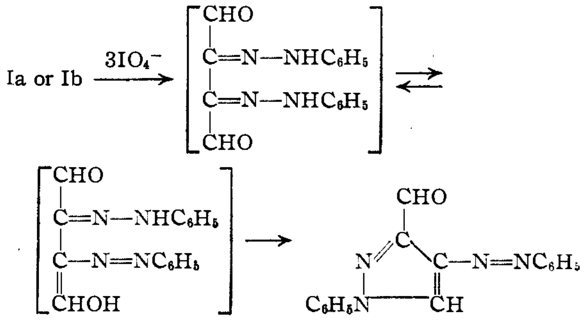
Ia



Ib

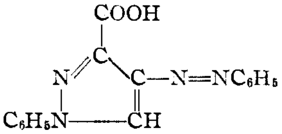
When the oxidation with periodic acid was carried out in a slightly alkaline alcoholic solution, a compound (II) was isolated in a yield of almost 80% whose analytical composition deviated from that of the 2,3-bis-phenylhydrazone of diketosuccinaldehyde, expected by analogy to the behavior of glucose phenylosazone,[5] by the lack of the elements of one molecule of water. The same substance was obtained, though in a lower yield, when the oxidation took place in acidic alcohol. The compound gave the Schiff test and could be oxidized by silver oxide under alkaline conditions to a monocarboxylic acid (III). With semicarbazide it yielded the corresponding semicarbazone.

Compound II appears, therefore, to be derived from the 2,3-bis-phenylhydrazone of diketosuccinaldehyde by the removal of one molecule of water and the concomitant suppression of one aldehyde function. The cyclodehydration of an enolic intermediate would account for the formation of 1-phenyl-4-phenylazo-3-pyrazolecarboxaldehyde (II) from the cyclohexose osazones. This reaction is analogous to the well known formation of 1-phenylpyrazoles from β-diketones and phenylhydrazine.[6]



II

The oxidation of II results in the formation of 1-phenyl-4-phenylazo-3-pyrazolecarboxylic acid (III).



III

The investigation of the absorption spectra of compounds II and III and of IIIa, the sodium salt of compound III, gave results favoring the structures discussed here (see Figure 1). The spectra of II and of the sodium salt IIIa were very similar, showing the low intensity "R band" (molecular extinction ϵ1060 and 940, at wave lengths of 425 and 435 mμ, respectively, obtained by graphical interpolation), and the high intensity "K band" in the ultraviolet, as found characteristic of phenylazo compounds.[7] The free acid III exhibited a slightly different spectrum, probably

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[1] This work was supported in part by a grant from the American Cancer Society on the recommendation of the Committee on Growth of the National Research Council.

[2] This report is from a dissertation to be submitted by Boris Magasanik in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University.

[3] E. Chargaff and B. Magasanik, *J. Biol. Chem.*, **165**, 379 (1946); B. Magasanik and E. Chargaff, *ibid.*, **174**, 173 (1948).

[4] The enantiomorphic osazones originating from *l*- and from *d*-inositol, *i. e.* compounds Ia and Ib, yielded, of course, the same oxidation product with periodic acid.

[5] E. Chargaff and B. Magasanik, THIS JOURNAL, **69**, 1459 (1947).

[6] H. Meyer, "Synthese der Kohlenstoffverbindungen", Wien, Vol. II, 1940, p. 891.

[7] A. Burawoy, *J. Chem. Soc.*, 1865 (1937); 1177 (1939).

reflecting contributions by the various tautomeric forms.

The reasons for the readiness with which the pyrazole was formed in the course of the oxidation of the cyclic osazone are not certain. A previous study from this Laboratory[5] has shown the action of periodic acid on the open-chain glucose phenylosazone to result in the production of the 1,2-bisphenylhydrazone of mesoxalaldehyde; there, an aldehyde group vicinal to an osazone structure was stable. It is possible that the farther-reaching transformation encountered in the present work had its origin in the cyclic nature of the osazone cleaved by periodic acid.

Experimental

1-Phenyl-4-phenylazo-3-pyrazolecarboxaldehyde (II).—A solution of 1.08 g. (3 millimoles) of compound I in 400 cc. of absolute ethyl alcohol was cooled to room temperature and treated with 2.06 g. (9 millimoles) of paraperiodic acid in 300 cc. of 1% aqueous sodium bicarbonate. After one hour the mixture, diluted with one liter of water, was three times extracted with ether. The crystalline evaporation residue of the combined ethereal extracts was recrystallized from aqueous alcohol when *compound II* was obtained as 650 mg. of long orange needles (78% of the theoretical yield). The substance melted[8] at 131°; it gave the Schiff test, was insoluble in water, alkali, and acid, soluble in organic solvents.

Anal. Calcd. for $C_{16}H_{12}ON_4$ (276.3): C, 69.5; H, 4.4; N, 20.3. Found: C, 69.2; H, 4.2; N (Dumas), 20.1.

When the oxidation with periodic acid was carried out in the absence of sodium bicarbonate, the pyrazole II was obtained in a yield of only 18%.

The **semicarbazone of II**, after several recrystallizations from ethanol–benzene and from ethanol, formed yellow needles, melting at 188–189° (dec.).

Anal. Calculated for $C_{17}H_{15}ON_7$ (333.4): C, 61.2; H, 4.5; N, 29.4. Found: C, 61.5; H, 4.2; N, 29.5.

1-Phenyl-4-phenylazo-3-pyrazolecarboxylic Acid (III).—To a mixture of 555 mg. of silver nitrate in 40 cc. of water and 415 mg. of compound II (1.5 millimoles) in 30 cc. of ethanol, 5 cc. of *N* potassium hydroxide was added dropwise with constant stirring in the course of ninety minutes.[9] The acidification of the filtrate brought about the separation of 280 mg. of the crude acid (64% yield). *Compound III*, following recrystallization from absolute ethanol, formed orange needles, melting at 196–197° (dec.), insoluble in water, soluble in warm aqueous sodium bicarbonate.

Anal. Calculated for $C_{16}H_{12}O_2N_4$ (292.3): C, 65.7; H, 4.1; N, 19.2; neut. equiv., 292. Found: C, 65.6; H, 3.8; N, 19.2; neut. equiv., 288.

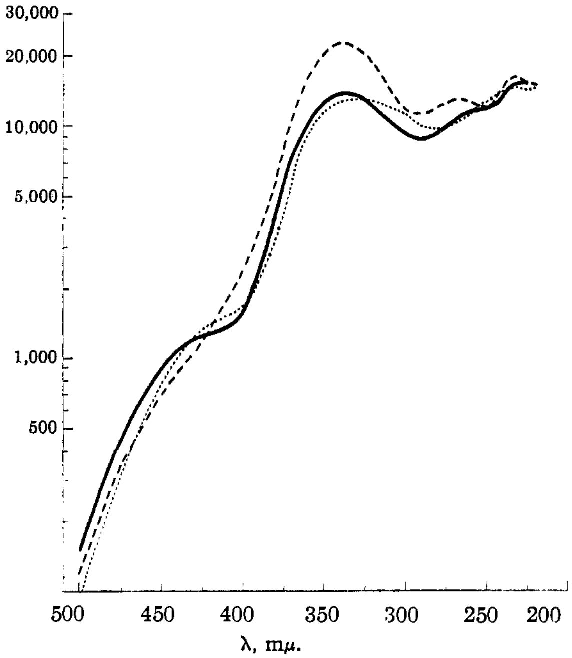

Fig. 1.—Absorption spectra (in absolute ethanol) of compounds II, III and the sodium salt IIIa: ——, IIIa Na salt; — — — — — —, III; .... II.

Absorption Spectra (Fig. 1).—The spectra of compounds II and III and of the sodium salt IIIa (prepared by the exact neutralization of III) were measured by means of a Beckman photoelectric quartz spectrophotometer. About 0.5 and 0.05 millimolar solutions in absolute alcohol were used for visual and ultraviolet spectroscopy, respectively.

The authors are grateful to Mr. W. Saschek and Miss R. Rother for the microanalyses.

Summary

The action of periodic acid on the cyclohexose osazones derived from *l*- and *d*-inositol leads to the formation of 1-phenyl-4-phenylazo-3-pyrazolecarboxaldehyde. Derivatives of this substance (semicarbazone and carboxylic acid) are described. The results of a study of the absorption spectra of these compounds bear out the structures assigned to them.

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[8] The melting points, reported without correction, were determined with an electrically heated stage (Fisher–Johns).

[9] M. Délépine and P. Bonnet, *Compt. rend. Acad. Sci.*, **149**, 39 (1909).