indicating that the excess of PAAH has been removed by the *n*-butyraldehyde treatment. The specific activity increased from 1.15 mμM. C^{14}-L-valine/mg. s-RNA in the initial mixture to 11.5 mμM. C^{14}-L-valine/mg. s-RNA for the final solution (based on an assumed molecular weight for C^{14}-L-valine s-RNA of 25,000). This corresponds to a ten-fold enrichment and a purity of 28%. (For a molecular weight of 30,000 this would represent a purity of 34%. The recovery of the unoxidized s-RNA including the enriched C^{14}-L-valine s-RNA is essentially 100%, but that of the counts is 80%, indicative of some dissociation of the amino acid. The procedure described here is highly reproducible and may be used for larger quantities. With the high yield attained it is evident that repetitions of this procedure should lead to high purity of single amino-acid acceptor s-RNA in useful amounts.

Recent investigations have shown that PAAH also reacts with oxidized nucleosides and nucleotides, to form stable hydrazones. Neither cleavage of the phosphoester bond nor the release of the corresponding bases could be observed in nucleotides or s-RNA at acid or neutral *p*H, as reported by Khym and Cohn[13] and Saponara and Bock,[9] who used phenylhydrazine derivatives. Thus this polymer should find other uses in nucleic acid chemistry.

We wish to acknowledge generous help in the initial stages of this work from Dr. Yoshimi Kawade and useful discussions with Professor P. C. Zamecnik. H.v.P. gratefully acknowledges the support of a NATO Fellowship. This work was supported in part by National Cancer Institute Grant C-2170 and in part by AEC Contract At (30-1)-2643.[14]

(13) J. X. Khym and W. E. Cohn, *J. Am. Chem. Soc.*, **82**, 6380 (1960).

(14) This is publication No. 1048 of the Cancer Commission of Harvard University.

DEPARTMENT OF CHEMISTRY AND
J. C. WARREN LABORATORIES HANS VON PORTATIUS
HARVARD UNIVERSITY PAUL DOTY
CAMBRIDGE, MASSACHUSETTS MARY L. STEPHENSON

RECEIVED JUNE 30, 1961

CHEMISTRY OF CHALCOSE, A 3-METHOXY-4,6-DIDEOXYHEXOSE

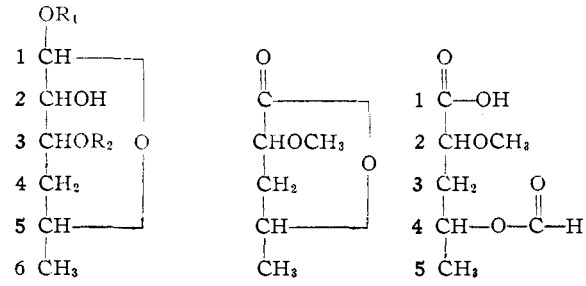
Sir:

Acid degradation of the antibiotic chalcomycin[1] has yielded chalcose (Ia), a 3-methoxy-4,6-dideoxyhexose. We wish to report the structural determination of this new sugar.

Methanolysis of chalcomycin yielded crystalline methyl chalcoside (Ib), m.p. 101.5–102°, $[\alpha]^{27}D$ −21° (*c* 2.04%, chloroform) [*Anal.* Calcd. for $C_8H_{16}O_4$: C, 54.53; H, 9.15; O, 36.32; C-CH_3 (1), 8.53; OCH_3 (2), 35.22. Found: C, 54.68; H, 9.25; O, 36.30; C-CH_3, 7.17; OCH_3, 33.7].

(1) Parke, Davis & Company, Belgian Patent 587,213, August 2, 1960.

Aqueous hydrolysis of methyl chalcoside gave crystalline chalcose (Ia), m.p. 96–99°, $[\alpha]^{24}D$ +120° (2 min.) → +97° (10 min.) → +76° (3 hr. and 26 hr.) (*c* 1.5%, water) [*Anal.* Calcd. for $C_7H_{14}O_4$: C, 51.84; H, 8.70; OCH_3 (1), 19.14. Found: C, 52.07; H, 8.93; OCH_3, 19.21], which could be reconverted to the crystalline methyl chalcoside by treatment with methanolic hydrogen chloride.



Ia, R_1 = H, R_2 = CH_3 II III
Ib, R_1 = R_2 = CH_3
Ic, R_1 = R_2 = H

Chalcose gave a positive Fehling test and a brown color with aniline hydrogen phthalate on papergrams. It reduced one mole of periodate, liberating no formaldehyde. Reduction of chalcose with sodium borohydride gave dihydrochalcose, which reduced one mole of periodate, liberating 0.7 mole of formaldehyde (chromotropic acid and dimedone methods). These data show that chalcose is a 2-hydroxy-aldosugar, as indicated by C_1 and C_2 of formula Ia.

Treatment of chalcose with fuming hydrobromic acid at 3° for 3 days[2] yielded de-O-methylchalcose (Ic), R_f 0.65 (chalcose R_f 0.70; *t*-butyl alcohol: acetic acid:water, 2:2:1). Treatment of Ic with two moles of periodate for 21 hours liberated (a), approximately one mole of acid (potentiometric titration), presumably formic acid from C_2 of formula Ic, and (b), crotonaldehyde (identified as the 2,4-dinitrophenylhydrazone), presumably formed by β-elimination of the oxygen function in 3-hydroxy(or 3-formyl)-butyraldehyde,[3] which originated from C_3 to C_6 of formula Ic. Both chalcose and dihydrochalcose gave slightly positive iodoform tests.

Oxidation of chalcose with periodate-permanganate[4] yielded a C-6 γ-lactone (II) (infrared absorption at 5.56 μ) and a crystalline C-7 acid (III), m.p. 68–69° [*Anal.* Calcd. for $C_7H_{12}O_5$ C, 47.72; H, 6.87; C-CH_3 (1), 8.53; OCH_3 (1), 17.62. Found: C, 48.00; H, 7.39; C-CH_3, 6.97; OCH_3, 16.99]. Treatment of the C-7 acid with 0.2 *N* sodium hydroxide resulted in the uptake of 2.02 equivalents of base, and gave after acidification, the same γ-lactone (II) mentioned earlier (identical infrared spectra). Reduction of the C-7 acid or the lactone with lithium aluminum hydride yielded an oily C-6 diol, characterized as its crystalline bis-3,5-dinitrobenzoate, m.p.

(2) K. Hess and F. Neumann, *Chem. Ber.*, **68B**, 1371 (1935).

(3) E. H. Flynn, M. V. Sigal, Jr., P. F. Wiley and K. Gerzon, *J. Am. Chem. Soc.*, **76**, 3121 (1954).

(4) R. U. Lemieux and E. von Rudloff, *Can. J. Chem.*, **33**, 1701 (1955).

124.5–127.5° [*Anal.* Calcd. for $C_{20}H_{18}O_{13}N_4$: C, 45.98; H, 3.47; N, 10.73; C-CH_3 (1), 2.88. Found: C, 45.83; H, 3.52; N, 10.86; C-CH_3, 3.02]. These data indicate the presence of a 4-formylbutyric acid skeleton in the C-7 acid. The n.m.r. spectrum[5] of the C-7 acid [(a) −5.84, acidic hydrogen; (b) −3.58, formyl hydrogen; (c) −0.69, C_2 hydrogen; (d) +0.84, C_4 hydrogen; (e) +1.24, singlet, O-methyl hydrogens; (f) +2.68, C_3 hydrogens; (g) +3.33, doublet (J = 6 cps.), C_5 hydrogens; ratios of areas 1:1:1:1:3:2:3, respectively] shows that III represents the only compatible manner of methyl and methoxyl substitution on this skeleton.

The structure of the γ-lactone from chalcose was confirmed as II by synthesis. Condensation of diethyl methoxymalonate[6] with allyl bromide in the presence of potassium *t*-butoxide gave diethyl allylmethoxymalonate, b.p. 106° (2.4 mm.), $n^{25}D$ 1.4362 [*Anal.* Calcd. for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.22; H, 8.07]. The ester was saponified, then treated with 50% sulfuric acid at 100° to give both pairs of diastereoisomers of α-methoxy-γ-valerolactone, one of which [*Anal.* Calcd. for $C_6H_{10}O_3$: C, 55.37; H, 7.75. Found: C, 54.95; H, 7.95] exhibited the same infrared spectrum and vapor phase chromatograms (170°) as the lactone from chalcose.

The structure of chalcose is thus proved to be Ia, a formulation which also has been confirmed by its n.m.r. spectrum.[7]

(5) Obtained in $CDCl_3$ solution at 40 mc. Chemical shifts given in parts per million relative to water as 0.

(6) D. E. Ames and R. E. Bowman, *J. Chem. Soc.*, 1079 (1951).

(7) Determined in $CDCl_3$ solution at 60 mc. by L. F. Johnson, Varian Associates.

RESEARCH DIVISION
PARKE, DAVIS & COMPANY
DETROIT 32, MICHIGAN

PETER W. K. WOO
HENRY W. DION
QUENTIN R. BARTZ

RECEIVED JUNE 13, 1961

BOOK REVIEWS

Toxic Phosphorus Esters. Chemistry, Metabolism, and Biological Effects. By RICHARD D. O'BRIEN, formerly Pesticide Research Institute, Canada Department of Agriculture, London, Ontario, and now Associate Professor of Insecticide Chemistry, New York State College of Agriculture, Cornell University, Ithaca, New York. Academic Press Inc., 111 Fifth Avenue, New York 3, N. Y. 1960. xii + 434 pp. 16 × 23.5 cm. Price, $14.50.

Since World War II, organophosphates with their extraordinary biological activity as inhibitors of cholinesterase have opened up a very rich and important field of investigation. The toxic phosphorus esters include the so-called "nerve gases," tabun, sarin and soman, but more significantly, the discovery of these toxic warfare agents led to the further discovery and development of extremely useful insecticides which are used now on a world-wide basis. Some of these insecticides possess systemic properties, *i.e.*, they penetrate the host plant or animal to kill the insects or arthropods attacking the host. Some of the toxic phosphates turned out to be excellent tools for the investigation of certain esterase enzymes, and this had led to new basic knowledge in enzyme chemistry. The author tells this absorbing story and tells it very well indeed. But his text is nonetheless disciplined, well indexed, and outstanding in the completeness of references which he gives at the end of each chapter. The reader can find what he is looking for.

The opening chapter outlines the plan of the book, the history of phosphorus esters, a brief exposition of the nomenclature of these compounds, with a sketch of what is known about cholinesterase and its biological significance. Chapter 2, entitled "Nonenzymic Reactions," describes the hydrolysis, isomerization, transalkylation, oxidation (sulfides to sulfoxides or sulfones, replacement of sulfur by oxygen), dehydrochlorination and effects of light on phosphates. Chapter 3 brings the phosphates into reaction with cholinesterase *in vitro* and describes the kinetics of this reaction and what is known about the relationship between the structure of the inhibitor and anticholinesterase activity. There is also a discussion on the reversal of inhibition and selective inhibition between true and pseudocholinesterase. Chapter 4 tells of enzyme reactions *in vitro* which either enhance or reduce the reactivity of the inhibitor. Chapter 5 describes inhibitor effects on nerve and muscle tissue, especially as they relate to mechanisms of nerve transmission. Chapter 6 gives a very good comprehensive treatment of the effects in mammals of poisoning, and it includes the counter-effects of atropine and of 2-PAM and other oximes which can be used as prophylactics or as antidotes. Also included in this chapter is a brief account of synergism or potentiation of certain phosphates, as well as the metabolism in intact animals of Co-Ral, diazinon, Delnav, dimethoate, Dipterex, malathion, parathion, Phosdrin, ronnel and Systox. Chapter 7 describes the effects of phosphate inhibitors in insects, ovicidal action, differential toxicity. It includes a brief summary of insect resistance to phosphates with a description of what is known about mechanisms of resistance. Chapter 8 gives an account of systemic effects of phosphates in plants and their metabolism. Chapter 9 carries the intriguing title "Selective Toxicity." If the synthesis chemist knew much about this subject, he could design compounds to kill harmful species of pests which would be perfectly safe to man and his livestock. This chapter necessarily contains much that is speculative; it also has some stimulating ideas and some solid data in it. Chapter 10 closes with an outline of some useful techniques which are especially appropriate to working with phosphates in the laboratory. An appendix includes a brief treatment of electronic effects which influence polarity, acidity and basicity of molecules. Included is a useful list of toxic phosphates (mostly insecticides or acaricides) giving the structure, common name and manufacturer.

This book is full of up-to-date information, and it is written in a very fine straightforward style. It is definitely a book to have if you are concerned at all with this important field of interest.

PESTICIDE CHEMICALS RESEARCH BRANCH
U. S. DEPARTMENT OF AGRICULTURE
BELTSVILLE, MARYLAND

S. A. HALL