constituent of the protoplasm, they will be transmitted to future generations of cells through cell division. Cell division will increase cellular surface area and consequently the available oxygen so that peroxides will again increase.

The free-radical oxidation chain can be broken by radioactive radiations, certain nitrogen compounds (carbamates, aryl amines, bis-β-chloroethyl substituted tertiary amines, alkyl ureas, etc.), quinones and similar compounds. Consequently, these agents inhibit cancer by retarding the oxidation. The oxidation can be probably completely prevented by lipoid-soluble iodides (quaternary aryl or alkyl ammonium iodides, iodogorgoic acid, etc.) and related materials because compounds of this sort are remarkably effective in destroying hydroperoxides. A free-radical, branched-chain oxidation reaction may be started in the tissues not only by carcinogenic hydrocarbons but also by ultraviolet light, X-rays and radioactive radiations, high temperature, etc. It should be possible to check the validity of the free-radical mechanism of cancer by studying the kinetics of the oxidation of cancerous tissue *in vitro*.

In some cases it would be possible to extract some of these hydroperoxides from the cells. They could then be filtered through a Berkefeld filter and injected into non-neoplastic tissue. Whereupon, if the injected hydroperoxides possess a low activation energy, they could decompose to form free-radicals and thus initiate another branched-chain oxidation reaction so that cancer would result. The hydroperoxide molecules also have the unique property of multiplying in the presence of oxygen and organic molecules containing hydrogen attached to secondary or tertiary carbon atoms. It is not surprising, therefore, that numerous investigators have mistaken these hydroperoxides for viruses.

Despite the pronounced superficial diversity of the multitude of neoplasms, the hydroperoxide theory might possibly be applicable to all types, not only carcinomas but also endotheliomas and sarcomas. It might even be applied with success to many kinds of benign hyperplasia.

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RECEIVED JULY 25, 1947

CRYSTALLINE DERIVATIVES OF 6-α-D-GLUCOPYRANOSIDO-β-D-GLUCOSE FROM STARCH

Sir:

Waxy corn starch (400 g.) was hydrolyzed with a purified amylolytic enzyme prepared from *Aspergillus oryzae*. Fermentable sugars were removed by treatment with bakers' starch-free yeast. Proteins were removed with basic lead acetate, and the liquors further purified by passage through Amberlite-resin exchange IR-4 and IR-100 ion columns. After concentration and treatment of the liquors with methyl, ethyl and butyl alcohols, an amorphous white solid (A) consisting essentially of the non-fermentable fragments of starch was obtained; reducing value 82% of that calculated for maltose monohydrate; $[\alpha]^{25}D$ + 127.6° (*c*, 2 in water); yield 6.3 g.

This solid (A) was esterified with *p*-nitrobenzoyl chloride in pyridine and yielded a crystalline product, presumably octa-*p*-nitrobenzoyl 6-α-D-glucopyranosido-D-glucose; diamond-shaped crystals; $[\alpha]D$ + 22.0° (*c*, 1.27 in acetonylacetone); m. p. 188°.

Anal. Calcd. for $C_{12}H_{14}O_{11}(OC_7H_4NO_2)_8$: C, 53.20; H, 3.02; N, 7.40. Found: C, 53.20; H, 3.27; N, 7.70.

On *acetylation* of solid (A) with acetic anhydride in pyridine at 0° a crystalline compound apparently 6-α-D-glucopyranosido-D-glucose octaacetate (I) was obtained in the form of brush-like clusters of needles; $[\alpha]^{25}D$ + 37° (*c*, 1.23 in chloroform); m. p. 175°.

Anal. Calcd. for $C_{12}H_{14}O_{11}(CH_3CO)_8$: C, 49.6; H, 5.63; CH_3CO, 50.7; mol. wt., 678.6. Found: C, 49.7; H, 5.48; CH_3CO, 50.6; mol. wt. (Rast), 670.

The sirup obtained by deacetylation of this acetate gave the same octa-*p*-nitrobenzoate described above.

In addition to these crystalline compounds, an amorphous octacetate had also been prepared at the time the Communication to the Editor by Georges, Miller and Wolfrom[1] appeared, describing the isolation of the octaacetate of 6-α-D-glucopyranosido-β-D-glucose following the acid hydrolysis of dextran. Our amorphous octaacetate was formed by acetylation of solid (A) with a solution of sodium acetate in acetic anhydride at 100 to 110°; $[\alpha]^{25}D$ + 96.2° (*c*, 2 in chloroform). This acetate has in the meantime crystallized; long prism-shaped crystals; $[\alpha]^{25}D$ + 98.2° (*c*, 1.50 in chloroform); m. p. 142°.

Anal. Calcd. for $C_{12}H_{14}O_{11}(CH_3CO)_8$: C, 49.56; H, 5.63; CH_3CO, 50.7. Found: C, 49.6; H, 5.73; CH_3CO, 50.9.

This acetate (II) has the same physical properties as the octaacetate of 6-α-D-glucopyranosido-B-D-glucose from dextran. The melting point of a mixture of the octaacetate derived from dextran, which was kindly supplied by Dr. Wolfrom, and octaacetate II from starch was 142°. Following Dr. Wolfrom's suggestion, X-ray powder diffraction diagrams of these compounds were taken, and also were found to be identical.

The two crystalline acetates prepared in this work behaved like 1,6- rather than 1,4-disaccharides toward hydrogen bromide in acetic anhydride and acetyl bromide, that is 1,4-disaccharides are ruptured to form acetobromo-monosaccharides, whereas 1,6-disaccharides are not, but in-

(1) L. W. Georges, I. L. Miller and M. L. Wolfrom, THIS JOURNAL, **69**, 473 (1947).

stead behave anomalously.[2] Thus a quantity of acetate in 10 ml. of a solution of hydrogen bromide in acetic acid and acetyl bromide, calculated to produce 7.576×10^{-4} mole of 1-bromotetraacetyl glucose, assuming the disaccharide is quantitatively converted to this derivative, gave the following end rotations: β-maltose octaacetate, +17.2; gentiobiose octaacetate, +12.2; and octaacetates I and II, + 12.1 and +11.2°, respectively.

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RECEIVED AUGUST 8, 1947

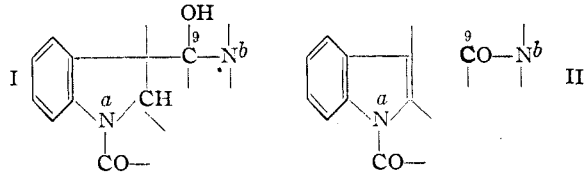
(2) Allene Jeanes and G. E. Hilbert, presented before the American Chemical Society, Sept. 11–15, 1944.

(3) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

THE STRUCTURE OF STRYCHNINE

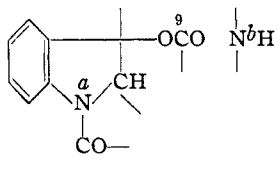
Sir:

We have found that the ultraviolet absorption spectrum [$\lambda\lambda_{max.}$ (log ϵ): 246(4.15), 270(3.92), 294(3.72)] of strychnone, the neutral product[1] of the action of acidic hydrogen peroxide on *pseudo*strychnine, resembles closely that of model N-acylindoles, and is entirely different from that of strychnine and other N-acyldihydroindoles. This observation can be accommodated on the basis of the change I → II. It is clear that in the

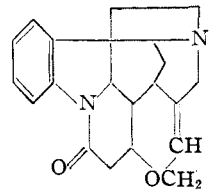


imino-carbonyl chain tautomer of I, the oxidizing agent interpolates an oxygen atom between the (potential) carbonyl group at C.9 and the β-carbon atom of the indole nucleus, giving III. The subsequent changes are unexceptional. The new expression leads to $-N^{a}H\ HOOC$ for strychnone hydrate. N^a is now part of an indole system, and in the hydrate is only very feebly basic, as required. Methoxydihydrostrychnone is simply the ester $-NH\ MeOOC$. Like other indoles and N-acylindoles, none of these substances gives, as do N-acyldihydroindoles, the characteristic Otto reaction.

The importance of these considerations is twofold: (i) on the new basis, the formation of strychnone is the long-sought crucial experiment with respect to resolving the remaining dubieties concerning the mode of the linkage of N^b to the indole ring. Consequently, taken with the recent observations of Robinson[2] on the environment of the double bond in the *neo* series, and similar studies in this Laboratory on the replacement by methylene of the ketonic group of methoxymethyl-*chano*dihydrostrychnone, the new evidence completes the inferential proof for a particular expression for strychnine, IV.[3] (ii) In the formation of strychnone, the very involved tightly fused polycyclic system of strychnine has been broken into to an extent not achieved in any of the extensive earlier degradations, which have in the main led only to the destruction of the periphery of the molecule. Thus, the way is now open to build up an unequivocal degradative proof of structure for strychnine.



III



IV

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(1) Leuchs, *et al.*, *Ber.*, **77**, 408 (1944).

(2) Chakravarti and Robinson, *Nature*, **160**, 18 (1947).

(3) This expression, which for some years has been considered independently in this Laboratory (*cf. J. Chem. Soc.*, 903 (1946), footnote, p. 904) and in that of Sir Robert Robinson (ref. 2), represents a slight modification of the structure regarded in 1939 by the latter (*J. Chem. Soc.*, 603 (1939)) as the culmination of the strychnine structure problem, on the basis of a long and brilliant logical sequence, much of which had been elaborated as early as 1930 (Robinson, *Proc. Roy. Soc. (London)*, **130A**, 431 (1931).