reduction in 50% aqueous acetic acid with zinc for forty-five minutes was sufficient for reductive removal of the trimethylammonium group from both methiodides. The two resulting desdimethylamino products were identical. Desdimethylaminotetracycline: $[\alpha]^{25}D$ −250° (0.5% in methyl cellosolve); m.p. 195° (dec.); *Anal.* Calcd. for $C_{20}H_{19}NO_8$: C, 59.75; H, 4.77; N, 3.49. Found: C, 59.80; H, 4.72; N, 3.30. "Desdimethylaminoquatrimycin": $[\alpha]^{25}D$ −251° (0.5% in methyl cellosolve); m.p., 195° (dec.); *Anal.* Found: C, 59.40; H, 4.88; N, 3.42. Mixed melting point showed no depression.[6]

This represents necessary and sufficient proof that the quatrimycins are the 4-*epi*tetracyclines.

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RECEIVED MARCH 5, 1956

THE BIOSYNTHESIS OF α, ε-DIAMINOPIMELIC ACID. I. ISOLATION OF AN INTERMEDIATE, ACTIVE FOR A DIAMINOPIMELIC ACID-REQUIRING *E. coli* MUTANT

Sir:

It has been well established[1] that α,ε-diaminopimelic (DAP) acid is found in many Gram-negative and some Gram-positive organisms. The biosynthetic mechanism of DAP synthesis is at present unknown and it is the purpose of this communication to report the isolation of a biologically active compound apparently formed as an intermediate in the biosynthesis of DAP.

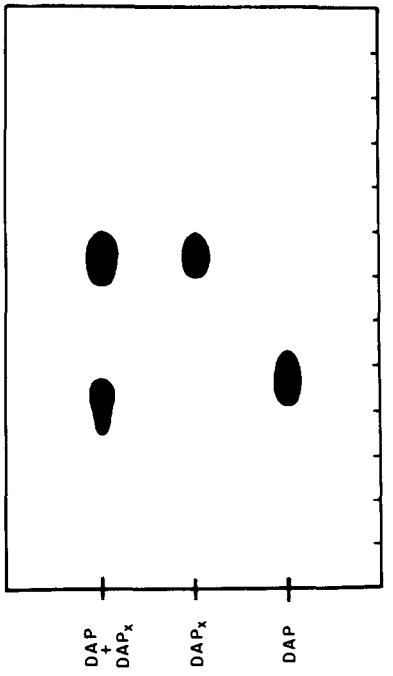
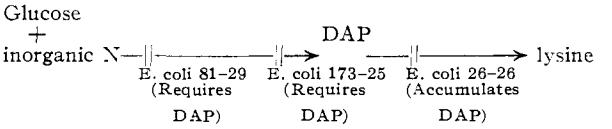


Fig. 1.—The chromatographic behavior of a material having growth-supporting activity for a DAP-requiring *E. coli* mutant: solvent, methanol (80), water (20), pyridine (4); temp. 25; descending system, Whatman No. 1 paper, bioautographic plate, using *E. coli* 81-29.

(1) E. Work and D. L. Dewey, *J. Gen. Microbiol.*, **9**, 394 (1953).

The biosynthesis of DAP can be accomplished by *E. coli*, using glucose as a sole source of carbon. Using the mutant[2] system illustrated below, it has been possible to isolate a preparation, active for a DAP-requiring mutant, *E. coli* 81–29.



This biologically active material was designated as DAP_x for convenience.

DAP_x is extracted from lyophilized *E. coli* 26–26 supernates at *p*H 3–5 with diethyl ether, methylene chloride and *n*-butanol. The solvents are removed *in vacuo* and the solids dissolved in water and freeze-dried to yield a yellowish-brown product. Chromatography of DAP_x in a methanol–water–pyridine system and subsequent analysis on a bioautographic plate (Fig. 1) demonstrated that the material was different from DAP.

The material was found to be ninhydrin-negative, heat stable and acidic in character. Countercurrent distribution using *n*-butanol and water at *p*H 3 yielded a highly active fraction which was obtained in a pure state by crystallization from *n*-butanol. The material was identified as succinic acid by its infrared spectrum and by comparison of the free acid (m.p. and mixed m.p. 187.5–188.5°) and its *p*-bromophenacyl ester (m.p. and mixed m.p. with 214–215°) authentic specimens.

Subsequent studies with *E. coli* 26–26 have shown that aspartic acid, succinic acid, pyruvic acid, triphosphopyridine nucleotide (TPN) and adenosine triphosphate (ATP) stimulate the synthesis of DAP by cell-free extracts. The stimulation of DAP synthesis by the compounds described above extend and confirm the report of Gilvarg[3] which appeared at the time this manuscript was in preparation.

Further studies on the biosynthetic mechanism of DAP synthesis are in progress and will be a subject of future publication.

(2) The three *E. coli* mutants were kindly obtained from Dr. B. Davis, New York University.

(3) C. Gilvarg, *Fed. Proc.*, 261 (1956).

RESEARCH LABORATORIES
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RECEIVED MAY 21, 1956

A NEW TWO STRANDED HELICAL STRUCTURE: POLYADENYLIC ACID AND POLYURIDYLIC ACID

Sir:

While studying the X-ray diffraction patterns of synthetic nucleotide polymers, we mixed together the sodium salts of polyadenylic acid and polyuridylic acid.[1] There resulted a very rapid

(1) M. Grunberg-Manago, P. J. Ortiz and S. Ochoa, *Science*, **122**, 907 (1955).

increase in viscosity as well as the drop in the optical density at 260 mμ which was reported recently by Warner.[2] From this viscous solution, tough, glassy fibers can be drawn which are negatively birefringent, $\Delta n = -0.10$.

These fibers produce a well-oriented X-ray diffraction pattern with a distribution of intensity which is characteristically helical. The helical pitch varies from about 32 Å. at low relative humidity to 36 Å. at high relative humidity. The molecules are packed in hexagonal array, with an intermolecular spacing varying from 26 Å. at low humidity to over 32 Å. at high humidity. From the strong near meridional reflections in the range 3.0–4.2 Å., it can be shown that the number of residues per turn is approximately ten. Thus, this diffraction pattern has many similarities to that exhibited by desoxyribose nucleic acid (DNA).[3] However, a major difference is found in the first layer line, which is very strong for this molecule, and quite weak for DNA.

We have interpreted these results in the following way. The molecule is a two-stranded helix containing one strand of polyadenylic acid and one of polyuridylic acid. The bases adenine and uracil make two hydrogen bonds with each other in the same manner as that postulated for adenine and thymine in DNA,[4] with the base pairs stacked above each other roughly perpendicular to the fiber axis. The strong first layer line indicates that the angular separation of the ribose-phosphate backbones viewed from the helical axis is less than in DNA. This may be due to a parallel arrangement of the backbones, or to an antiparallel arrangement (as has been postulated for DNA) but with a greater radius than exists in the DNA molecule. It is anticipated that further studies of the Fourier transforms of these alternatives will permit us to decide between them.

These results show for the first time that it is possible for the ribonucleic acid (RNA) backbone to assume a configuration not unlike that found in DNA, using the same complementarity in the base pairs. This implies that there may exist a form of the RNA molecule similar to that of DNA and that this could be the form in which RNA carries out its implied molecular duplication in the plant and smaller animal viruses.

Finally, we would like to point out that this method for forming a two-stranded helical molecule by simply mixing two substances can be used for a variety of studies directed toward an understanding of the formation of helical molecules utilizing specific interactions.

We would like to thank Professor S. Ochoa for supplying us with some of the polynucleotide polymers used in this work, and Dr. F. H. C. Crick for helpful discussion.

(2) R. C. Warner, *Fed. Proc.*, **15**, 379 (1956).

(3) M. H. F. Wilkins, A. R. Stokes and H. R. Wilson, *Nature*, **171**, 738 (1953); R. E. Franklin and R. G. Gosling, *ibid.*, **171**, 740 (1953).

(4) J. D. Watson and F. H. C. Crick, *ibid.*, **171**, 737 (1953).

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RECEIVED JUNE 8, 1956

THE ENZYMATIC SYNTHESIS OF RUBBER[1]

Sir:

Studies of the mechanism of biosynthesis of rubber in seedlings and cultured tissues of guayule have established that the carbon of the isoprenoid chain can be derived exclusively from acetate[2]; and flax enzyme preparations have indicated that the branched chain acids, β-methylcrotonate and β-methyl β-hydroxyglutarate are probable intermediates in the formation of the basic isoprenoid unit.[3] However, the requirement for intact plants or tissue cultures has made detailed studies of rubber biosynthesis difficult. We have now observed that incubation of latex with C^{14}-labeled acetate results in the incorporation of radioactivity into rubber. Latex, which may be obtained in quantity by "tapping" of *Hevea brasiliensis* bark, is a viscous cell-free liquid containing rubber particles, proteins and particulate cellular components, and constitutes the raw material for the natural rubber of commerce.

The time course of incorporation of acetate into rubber is shown in Fig. 1. Following incubation,

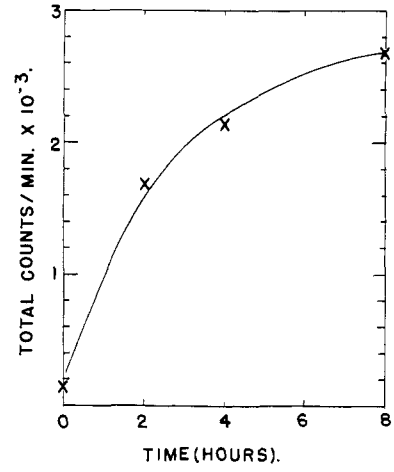

Fig. 1.—Time course of incorporation of 1-C^{14}-acetate into rubber: each incubation tube contained in micromoles, adenosine triphosphate 1, magnesium fructose diphosphate 2, CoEnzyme A 0.01, diphosphopyridine nucleotide 0.01, ethylenediamine tetraacetate 1, potassium phosphate 1, sucrose 60, acetate 2 (containing approximately 5×10^6 c.p.m.), and latex 0.1 ml.; total volume 0.3 ml.; *p*H 7; incubation at 37° for the indicated time.

the latex reaction mixture was coagulated with acetone and the rubber purified for counting by acetone and water extraction, solution in benzene–trichloroacetic acid, and precipitation as the micro-crystalline rubber bromide $(C_5H_8Br_2)_n$. The addition of cofactors, as listed in the legend for Fig. 1, stimulated the rate of acetate incorporation into rubber approximately ten-fold. Latex was also incubated with C^{14}-labeled sucrose, carbon

(1) Contribution jointly from Field Crops Research Branch, Agricultural Research Service, U. S. Department of Agriculture and Michigan State University, under contract with Quartermaster Corps., United States Army, using facilities at the Federal Experiment Station, Mayaguez, Puerto Rico.

(2) J. Bonner and B. Arreguin, *Arch. Biochem.*, **21**, 109 (1949).

(3) J. A. Johnston, D. W. Racusen and J. Bonner, *Proc. Nat. Acad. Sci.*, **40**, 1031 (1954).