

elution with hot 60% ethanol solution; (3) continuous extraction by diethyl ether from acid aqueous solution; (4) partition of the brucine salt between chloroform and water, the activity appearing in the aqueous phase; (5) conversion of the brucine salt into the calcium salt; (6) fractionation of the latter by the procedures of Williams and co-workers [(THIS JOURNAL, 60, 2719 (1938)].

By these means 510 mg. of white, varnish-like calcium salt (corresponding to Williams' fraction "C") was obtained from an extract derived from 160 kg. of liver. This material was fed in amounts averaging 8 mg. per week to each of six albino rats receiving a vitamin B-free diet supplemented by thiamin, flavin and the alkali-hydrolyzed eluate from fuller's earth adsorbate of liver extract. The average gain in weight for each week was as follows: (1) 13.4 g., (2) 19.1 g., (3) 18.8 g. The animals of a control group receiving the same basal diet and supplements, but without the calcium salt preparation, gained on the average as follows: (1) 6.5 g., (2) 4.5 g., (3) 4.2 g. The calcium salt preparation therefore actively stimulates rat growth.

Through the kindness of Dr. Leo Rane the calcium salt preparations were tested for their ability to stimulate the growth of *Streptococcus hemolyticus* and the diphtheria bacillus. They were found to behave like pantothenic acid preparations in stimulating the growth of both microorganisms. For these reasons it appears likely that pantothenic acid is one of the substances, in liver extracts, which are necessary for rat growth.

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Y. SUBBAROW  
G. H. HITCHINGS

RECEIVED APRIL 24, 1939

**PANTOTHENIC ACID AS A GROWTH FACTOR FOR  
THE DOCHEZ NY5 STRAIN OF HEMOLYTIC  
STREPTOCOCCUS**

Sir:

A medium composed of gelatin hydrolyzate, amino acids, inorganic salts, glucose plus such accessory factors as glutathione, thiochrome, nicotinic acid, betaine, flavin, and glucosamine in the presence of a calcium-alcoholic precipitate of a highly purified liver extract provides almost optimum conditions for the growth of the Dochez

NY5 strain of hemolytic streptococcus [L. Rane, and Y. Subbarow, *Proc. Soc. Exp. Biol. Med.*, **38**, 837-839 (1938)]. We have found that the further addition of uracil, guanylic acid, xanthine, hypoxanthine, nicotinic acid amide in place of nicotinic acid, and a fraction of liver extract as yet unidentified may also be of significance in the growth of this strain of hemolytic streptococcus.

Certain similarities in the isolation and properties of the unknown factor in the liver extract and pantothenic acid suggested the possibility of substitution. Pantothenic acid "U-6000, ca. 50%," kindly supplied by Dr. R. J. Williams, has been tried. Pantothenic acid is active in the growth of the Dochez NY5 strain of hemolytic streptococcus, as indicated in the table. The amount of growth was equal to that obtained with the calcium-alcoholic precipitate of liver extract as described in our previous publication.

Pantothenic acid per 10 cc. basal medium, $\gamma$	100	50	25	10	5	2.5	1	0.5
Nephelometer reading (cf. L. Rane, and Y. Subbarow, — <i>loc. cit.</i> )	2.9	2.9	2.8	2.8	2.8	2.9	3.5	>4.7
Control, growth of organism in meat infusion broth	2.3							

It is of additional interest that a product synthesized in collaboration with G. H. Hitchings of the Harvard School of Public Health is able to replace pantothenic acid in an otherwise chemically-defined medium. The compound was made by the conjugation of  $\beta$ -alanine ethyl ester with the acyl chloride of acetylated  $\alpha,\delta$ -dihydroxyvaleric acid. The dihydroxyvaleric acid was obtained by the deaminization of *d*-ornithine. However, the material so prepared was needed in larger amounts than was pantothenic acid.

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Y. SUBBAROW

LEO RANE

RECEIVED APRIL 24, 1939

**REACTION OF NEOPENTYL CHLORIDE WITH  
SODIUM**

Sir:

We have isolated from the reaction of one mole of neopentyl chloride and sodium, a 13% yield of 2,2,5,5-tetramethylhexane, b. p. 135° at 736 mm.,  $n_D^{20}$  1.4049, a 36% yield of neopentane, f. p. -19 to -20°, b. p. 8.3° at 720 mm., and 17.6 g. of a

substance, b. p. 19.8° at 740 mm.,  $n_D^{20}$  1.3656,  $d_4^{14}$  0.6681. This substance dissolved in 66% sulfuric acid at 0° within ten minutes and did not decolorize a dilute alkaline permanganate solution within twenty-four hours. These properties correspond with those reported for 1,1-dimethylcyclopropane (Gustavson and Popper, *J. prakt. Chem.*, (2) **58**, 458 (1898)); the yield corresponds to 25%

Because of similarity in physical constants, the possibility of this compound being isopropylethylene was recognized. A known sample of isopropylethylene, prepared from isoamyl chloride and alcoholic potassium hydroxide, had the prop-

erties b. p. 18.8° at 731 mm.,  $n_D^{20}$  1.3640,  $d_4^{15}$  0.6332. It was insoluble in 66% sulfuric acid and decolorized a dilute alkaline permanganate solution instantly under the same conditions as used for the 1,1-dimethylcyclopropane above.

The significance of these results for the current theory of intramolecular rearrangement, especially in relation to the formation and behavior of free radicals, will be discussed in a separate paper.

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FRANK C. WHITMORE  
A. H. POPKIN  
J. R. PFISTER

RECEIVED APRIL 21, 1939

## NEW BOOKS

**Vitamin B<sub>1</sub> (Thiamine) and its Use in Medicine.** By ROBERT R. WILLIAMS, Sc.D., Bell Telephone Laboratories, and TOM D. SPIES, M.D., Associate Professor of Medicine, University of Cincinnati. The Macmillan Company, 60 Fifth Avenue, New York, N. Y., 1938. xvi + 411 pp. 19 figs. 16 × 24.5 cm. Price, \$5.00.

A very excellent Macmillan Medical Monograph presenting a history of the discovery of vitamin B<sub>1</sub> (Thiamine), its function in the regulation of cell respiration, and other physiological data, which are of immediate interest to clinicians and practicing physicians. It is an inspiring story of medical and biochemical progress beginning with the Chinese description of the disease beriberi—in the early centuries, and revealing the successive contributions of workers during years of scientific research finally leading up to the determination of structure and complete synthesis of the neutral vitamin substance by American investigators.

The authors have summarized the present knowledge of this important chemical substance in convenient form for future reference. In Part I are recorded data that are of the greatest interest and value to all practitioners of medicine. Particular attention is paid by the authors to the clinical considerations of practical interest and importance; to the relation of beriberi to similar diseases, the pathology and physiology of vitamin B<sub>1</sub>, its pharmacology, the methods of prevention and treatment of vitamin B<sub>1</sub> deficiencies and the relation of diet to beriberi disturbances.

In Part II the authors have presented a very complete survey of the chemical and biological literature dealing with vitamin B<sub>1</sub>. This embraces a review of its discovery, the methods of isolation and identification from natural sources, the determination of constitution and its final synthesis. The authors review also in this part the nature of the functional groups of the vitamin B<sub>1</sub> molecule; the

adopted methods of biochemical analysis, and discuss the present conclusions of physiologists regarding thiamine requirements in nutrition, and its general distribution in the living organism. Thiamine is one of several organic substances which play a vital role in living cells. The authors have brought together a large amount of scientific data of immediate interest to chemists, physicians, clinicians, physiologists and biologists. They deserve much credit for their method of presentation and its completeness. A most commendable feature of the book are the excellent bibliographies introduced at the end of each chapter.

TREAT B. JOHNSON

**Feuerfeste Baustoffe silikatischer und silikalthaltiger Massen.** (Refractory Materials of Construction Made up of or Containing Silicates.) By Dr.-Ing. Dr. Phil. CLAUS KOEPPPEL. Verlag von S. Hirzel, Königstrasse 2, Leipzig C 1, Germany, 1938. xvi + 296 pp. 51 figs. 15 × 23 cm. Price, RM. 15.50; bound, RM. 17.

This is Band 18 of "Chemie und Technik der Gegenwart" ("Modern Chemistry and Technology"). The author's purpose, freely translated, is "to help both the student and the practical man to orient himself in the wide-extending field of the silicate sciences with particular reference to their application to current practice in the manufacture and handling of refractory materials of construction." The book will be much easier reading for the experimental chemist than for either the student or the practicing ceramist, for the language is that of the scientist rather than the technician or the engineer. Nevertheless, the plan of treatment indicated above is carried out quite thoroughly.

The principal emphasis is on the properties and reactions of pure silica. This body of knowledge not only is