ered unchanged in quantitative yield. The second crop of crystals from the reaction of the *i*-ether had the properties of a mixture, indicating incomplete conversion and/or competition between methoxyl and propoxyl groups.

The preparation of cholesteryl halides from the *i*-ether and hydrogen halides under mild conditions[3] is not without analogy to the above. Wallis and co-workers, who have presented the currently most reasonable structure for the *i*-cholesterol compounds, considered[3c] that the interesting formation of the *i*-cholesterol compounds from the tosyl ester of cholesterol could best be described by a formulation which involves a molecular rearrangement. The essential nature of the reaction would now appear to involve an electronic shift between rings A and B with carbon atom no. 5 as the pivot.

A detailed description of the work which assumes interest as a preparative method as well as a presumptive route to the introduction or removal of labels in biochemical work will be reported later.

DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY
THE JOHNS HOPKINS UNIVERSITY
SCHOOL OF MEDICINE HERBERT MCKENNIS, JR.
BALTIMORE 5, MARYLAND

RECEIVED AUGUST 21, 1947

FORMATION OF QUINONE BY THE ACTION OF BROMINE OXIDE ON BENZENE

Sir:

In an attempt to elucidate the mechanism of the effect of oxygen in accelerating the bromination of hydrocarbons, the effect of bromine oxide (Br_2O) on the bromination of toluene and cyclohexane was investigated. This substance proved to be a powerful inhibitor for the photobromination of toluene (one mole per cent. of Br_2O in Br_2 reduced the rate of bromination to one-half; two and a half mole per cent. reduced the rate to 1/30). It showed no similar effect on cyclohexane. By comparing the total bromine content of the solution with its oxidizing power as determined by a titration with sodium arsenate, it has been shown that when bromine oxide (Br_2O), dissolved in carbon tetrachloride is mixed, in the light or in the dark, with toluene or cyclohexane, it is decomposed within one or two minutes. Attempts were then made to isolate the compounds formed by the reaction of bromine oxide with the hydrocarbons. When the unreacted bromine and excess solvent were removed from the reaction mixture containing toluene, a yellow concentrate was obtained which acted as an inhibitor in the bromination of toluene. It liberated iodine from acidified potassium iodide and reduced Tollens reagent instantaneously at room temperature. This behavior suggested a quinone. However, all attempts to isolate toluquinone failed.

When benzene was used, the yellow oil (which remained after the removal of the solvent and unreacted materials) liberated iodine from potassium iodide, reduced Tollens reagent, and had a characteristic quinone odor. The material was molecularly distilled at reduced pressure. The yellow crystals, thus obtained, melted at 111–113°, and did not depress the melting point of an authentic sample of *p*-benzoquinone. The residue still reduced Tollens reagent and liberated iodine from potassium iodide. It was moderately soluble in water in which it formed a pink solution, suggestive of *o*-benzoquinone; but attempts to isolate this compound have thus far met with no success.

The direct formation of quinone from benzene is most remarkable. It is one of the few instances known to the authors, whereby, in a single reaction, benzene is converted to quinone. The study of other halogen oxides is contemplated.

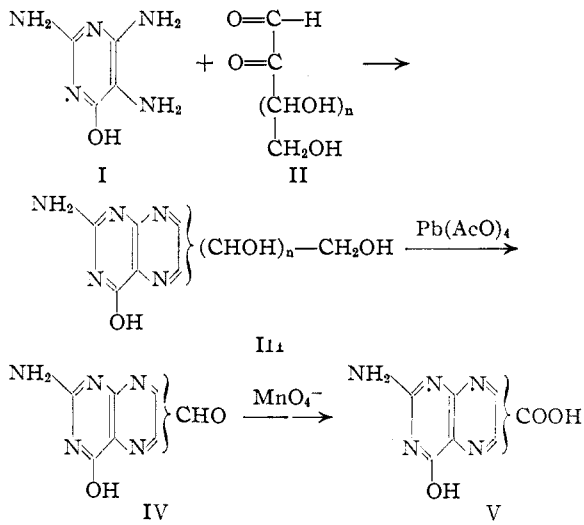
DEPARTMENT OF CHEMISTRY M. S. KHARASCH
UNIVERSITY OF CHICAGO PERCY B. POLEN
CHICAGO, ILLINOIS W. H. URRY

RECEIVED OCTOBER 6, 1947

A NEW SYNTHETIC METHOD FOR PTERINES

Sir:

In view of the recent publication of Karrer, *et al.*,[1] on the synthesis of polyhydroxypterines by the condensation of sugars with 2,3,5-triamino-6-hydroxypyrimindine (I) we wish to report our observations on the same reaction and on a new synthesis for similar compounds which is outlined below.



In our hands the condensation of D-glucose with I under the conditions of Karrer, *et al.*, yields 7-tetrahydroxybutylpterine, while the condensation of D-glucose with I-bisulfite or I-bisulfate under strongly acidic conditions yields primarily 6-tetrahydroxybutylpterine. The type of isomer obtained is determined by the physical properties of III or the carboxy-pterine (V) obtained from it.

(1) Karrer, Schwyzer, Erden and Siegwart, *Helv. Chim. Acta*, **30**, 1031 (1947).

Since the yield of 6-tetrahydroxypterine by the above procedure was small, our attention was centered on the more direct synthesis of III by the condensation of I with osones (II). The reaction of I with II is rapid and yields III in good quantity. The conditions for obtaining the preferred isomer appear to be reversed from that described above—*i. e.*, I and II at *p*H 5–9 yield the 6-isomer, while the condensation of I-bisulfite and II in strongly acidic solution yields a mixture richer in the 7-isomer.

Although details of work on pure isomers will be published later it is deemed worthy to report the synthesis of the isomeric mixture of III and the preparation of the isomeric mixture of formylpterine (IV) from III by the method outlined.

D-Glucosone was heated with an equivalent amount of 2,4,5-triamino-6-hydroxypyrimidine bisulfite in 75% acetic acid at 75° for forty-five minutes. The mixture was cooled and the precipitate collected. The product was exhaustively extracted with hot alcohol and dried. Yield of III was 60%, $[\alpha]^{26}_{D}$ −70.9° (169.2 mg. per 100 ml. of *N* NaOH). Absorption spectrum in 0.1 *N* NaOH showed maxima at 252 mμ and 360–362 mμ with ε of 19,000 and 7940, respectively.

Anal. Calcd. for $C_{10}H_{13}N_5O_5$: C, 42.39; H, 4.62; N, 24.71. Found: C, 42.17; H, 4.92; N (Kjeldahl), 25.11.

III was oxidized with lead tetraacetate to IV, an isomeric mixture, obtained in 85% yield. IV contained ash which was hard to remove. It exhibited strong carbonyl activity forming oximes, hydrazones and Schiff bases readily. IV treated with a slight excess of barium permanganate gives V, identity of which was established by its ultraviolet absorption, titration curve and analysis.

Anal. Calcd. for $C_7H_5N_5O_2H_2O$: C, 40.2; N, 33.5. Found: C, 38.8; N (Kjeldahl), 31.5 (cor. for 4.90% ash).

THE UPJOHN COMPANY H. G. PETERING
KALAMAZOO, MICHIGAN D. I. WEISBLAT

RECEIVED AUGUST 18, 1947

ANTAGONIST FOR PTEROYLGLUTAMIC ACID

Sir:

We wish to report the synthesis of a potent pteroylglutamic acid antagonist, N-[4-{[(2,4-diamino-6-pteridyl)-methyl]-amino}-benzoyl]-glutamic acid. In the course of an investigation of analogs of pteroylglutamic acid, this compound was prepared from 2,4,5,6-tetraminopyrimidine sulfate,[1] 2,3-dibromopropionaldehyde, and *p*-aminobenzoylglutamic acid under the conditions described for the synthesis of pteroylglutamic acid.[2] Purification of the crude product was accomplished by a method very similar to that used for pteroylglutamic acid.[3]

The purified product was obtained crystalline as clusters of yellow needles, and in 0.1 *N* sodium hydroxide solution it shows ultraviolet absorption maxima at 260, 284 and 370 mμ, and minima at 239, 271 and 333 mμ. *Anal.* Calcd. for $C_{19}H_{20}O_5N_8 \cdot 2H_2O$: C, 47.9; H, 5.1; N, 23.5. Found: C, 47.3; H, 5.18; N, 23.4. Magnesium salt: Calcd. for $C_{19}H_{18}O_5N_8Mg \cdot 3H_2O$: C, 44.2; H, 4.7; N, 21.7; Mg, 4.7. Found: C, 44.6; H, 4.85; N, 21.4; Mg, 4.82. The biological properties have been examined by Dr. B. L. Hutchings and Dr. E. L. R. Stokstad of the Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York. The inhibition ratio for half-maximum inhibition of the growth of *Streptococcus faecalis R* is 1.9, 0.7 and 0.4 at concentrations of pteroylglutamic acid of 0.003, 0.005 and 0.01 microgram per 10 ml., respectively.

Details of the synthesis and properties of this and related compounds will be the subject of subsequent communications.

CALCO CHEMICAL DIVISION DORIS R. SEEGER
AMERICAN CYANAMID COMPANY JAMES M. SMITH, JR.
BOUND BROOK, NEW JERSEY MARTIN E. HULTQUIST

RECEIVED SEPTEMBER 19, 1947

BIOSYNTHESES INVOLVING PANTOTHENIC ACID

Sir:

In *Escherichia coli* cysteic acid appears to prevent competitively the decarboxylation of aspartic acid to β-alanine which results in pantothenic acid becoming a limiting growth factor.[1] Under our testing conditions the rate of pantothenic acid synthesis is determined by the ratio of cysteic to aspartic acid, and exogenous substances allowing growth to occur at a lower rate of pantothenic acid synthesis produce an increased antibacterial index.[2]

Such an effect is obtained with citric, *cis*-aconitic or α-ketoglutaric acids. The antibacterial index over a thirty-fold range in aspartic acid concentrations was 300 in the medium containing these substances but only 30 in their absence. Oxalacetic and pyruvic acid were inactive alone, but a mixture of both necessitated a slight increase in the concentration of cysteic acid to obtain the same growth inhibition. Acetate alone possessed some activity. Pantoic acid was inactive. The apparent "sparing action" of *cis*-aconitic acid on the pantothenic acid requirement of *E. coli* is not equaled by its precursors; hence, it appears that pantothenic acid deficient cells are unable to convert effectively pyruvate and oxalacetate to *cis*-aconitate (or ketoglutarate). This datum explains the previously reported[1] enhanced activity of glutamic over aspartic acid in preventing the toxicity of cysteic acid. The transamination reaction produces both aspartic and α-ketoglutaric acids, the latter having a

(1) Traube, *Ber.*, **37**, 4545 (1904).
(2) Angier, *et al.*, *Science*, **103**, 667 (1946).
(3) Waller, *et al.*, THIS JOURNAL, **69**, in press (1947).

(1) Ravel and Shive, *J. Biol. Chem.*, **166**, 407 (1946).
(2) Molar ratio (analog to metabolite) just necessary for maximum inhibition of growth.