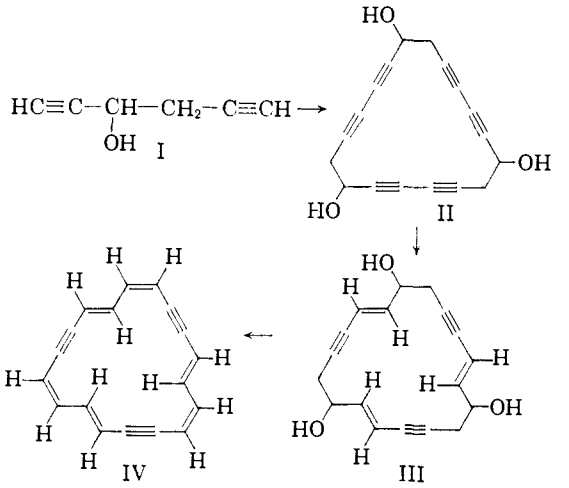
cyclic products to partial reduction and dehydration. We have now found that this type of sequence can be carried out successfully and by its use we have effected a second synthesis of the fully conjugated cycloöctadeca-1,7,13-(*cis*)-triene-3,9,-15-(*trans*)-triene-5,11,17-triyne (IV) already described.[1]

1,5-Hexadiyn-3-ol (I) [b.p. 72–73° (20 mm.), $n^{25}D$ 1.4755; found: C, 75.96; H, 6.56; acetylenic H, 2.06] was prepared in 50–60% yield by the reaction of propargylaldehyde with propargylmagnesium bromide[3a] or with propargyl aluminum bromide[3b] at −30 to −10°. The conditions are critical (details will be given in the full paper) and



1,4-hexadiyn-3-ol [HC≡C—CH(OH)—C≡C—CH_3] [b.p. 82–84° (20 mm.), $n^{25}D$ 1.4765; found: C, 76.57; H, 6.59; acetylenic H, 1.04] is formed when the reaction with propargyl magnesium bromide is carried out at 20°.

Oxidative coupling of I with cupric acetate in pyridine[2] (2.5 hr., 40°) gave a brown amorphous poly-ol containing α-diacetylene groupings ($\lambda_{max.}^{MeOH}$ 231, 244, 251 and 257 mμ; ε = 610, 920, 1020 and 1120, per C_6 unit). The infrared spectrum of the corresponding poly-acetate indicated it to be partly cyclic, as judged by the relative intensities of the α-diacetylene and terminal acetylene bands. By analogy[2] the poly-ol therefore presumably contains the symmetrical cyclic trimer II (two racemic forms possible) as well as other cyclic products. Attempts to purify the poly-ol (or the derived acetate or tetrahydropyranyl ether) were unsuccessful and often resulted in explosive decomposition, even at room temperature.

The poly-ol (or derivatives) could not be partially hydrogenated catalytically, but reduction with lithium aluminum hydride in boiling tetrahydrofuran yielded a brown mass with spectral data [$\lambda_{max.}^{MeOH}$ 228 mμ (ε = 11,000 per C_6 unit); $\lambda_{max.}$ 10.44 μ] compatible with the presence of *trans*-enyne chromophores. This method usually causes reduction only of acetylenic bonds adjacent to hydroxyl groups to *trans*-double bonds[4] and the mixture is therefore presumed to contain the triene-triyne-triol III besides other substances. Finally dehydration with phosphorus oxychloride–pyridine at 20° or with potassium bisulfate in boiling acetic anhydride–acetic acid gave a material which without purification showed the ultraviolet maxima at 322, 335, 384 and 399 mμ (isoöctane) typical of the fully conjugated hexaene-triyne IV[1]. Chromatography yielded IV as sole crystalline material, brown plates, m.p. 190–192° (dec.). It was identified with the previously described substance[1] by the complete identity of the infrared and ultraviolet spectra as well as by hydrogenation to cycloöctadecane. The crude poly-ol prior to lithium aluminum hydride reduction under the same dehydration conditions gave no material with high-intensity ultraviolet absorption.

The presently described synthesis of the completely conjugated eighteen-membered ring hexaene-triyne provides additional evidence for the structure IV.[1] The over-all yield by this new route is, however, inferior to that given by the previous method[1] which is a better one from the preparative standpoint.

DANIEL SIEFF RESEARCH INST. FRANZ SONDHEIMER
WEIZMANN INSTITUTE OF SCIENCE YAACOV AMIEL
REHOVOTH, ISRAEL YEHIEL GAONI

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(3) *Cf.* (a) M. Gaudemar, *Ann. chim.* (*Paris*), 190 (1956); (b) 204 (1956).

(4) *Inter al.*, J. D. Chanley and H. Sobotka, THIS JOURNAL, **71**, 4140 (1949); K. R. Bharucha and B. C. L. Weedon, *J. Chem. Soc.*, 1584 (1953); E. B. Bates, E. R. H. Jones and M. C. Whiting, *ibid.*, 1854 (1954).

THE ENZYMATIC SYNTHESIS OF ANTHRANILIC ACID FROM SHIKIMIC ACID-5-PHOSPHATE AND L-GLUTAMINE[1]

Sir:

Anthranilic acid, an intermediate in the biosynthesis of tryptophan in microörganisms,[2,3] has been shown to be derived from shikimic acid.[4,5] It has now been possible to demonstrate, in a cell-free extract of *Escherichia coli* mutant B-37,[6] that shikimic acid-5-phosphate[7,8] (I) and L-glutamine are converted to anthranilic acid (Table I).

Of all the amino donors tried, L-glutamine was the most effective. In addition, aza-L-serine and 6-diazo-5-oxo-L-norleucine, known inhibitors of reactions in which L-glutamine participates,[9] inhibit the present conversion. With L-glutamine as the amino donor shikimic acid alone was ineffective, and addition of ATP gave only a conversion of 18% in contrast to the almost quantitative conversion of shikimic-5-P.[10] Compound Z1 (prob-

(1) This work was supported by a grant from the National Institutes of Health, United States Public Health Service.

(2) C. Yanofsky, in "Amino Acid Metabolism" (W. D. McElroy and B. Glass, eds.), The Johns Hopkins Press, Baltimore, Md., 1955, pp. 930–939.

(3) C. Yanofsky, *J. Biol. Chem.*, **224**, 783 (1957).

(4) B. D. Davis in *Advances in Enzymology*, **16**, 287–295 (1955).

(5) E. L. Tatum, S. R. Gross, G. Ehrensvärd and L. Garnjobst, *Proc. Natl. Acad. Sci.*, **40**, 271 (1954).

(6) A tryptophan requiring mutant blocked in the conversion of anthranilic acid to indole-3-glyceryl phosphate.

(7) U. Weiss and E. S. Mingioli, THIS JOURNAL, **78**, 2894, 1956.

(8) Abbreviations: shikimic acid-5-phosphate, shikimic-5-P; Tris, 2-amino-2-hydroxymethyl-1,3-propanediol; ATP, adenosine triphosphate; DPN^+, DPNH, oxidized and reduced form of diphosphopyridine nucleotide; TPN^+, triphosphopyridine nucleotide; SA, shikimic acid.

(9) B. Levenberg, I. Melnick and J. M. Buchanan, *J. Biol. Chem.*, **225**, 163 (1957).

(10) Presumably these extracts can phosphorylate SA, albeit poorly.

TABLE I

SYNTHESIS OF ANTHRANILIC ACID FROM SHIKIMIC-5-P AND L-GLUTAMINE

Cell-free extracts were prepared by subjecting cells of freshly harvested *E. coli* mutant B-37 to sonic vibration.[11] The incubation mixtures contained 0.2 ml. of extract (4 mg. of protein), 5 μmoles of $MgCl_2$, 40 μmoles of Tris buffer *p*H 8.2, 1.0 μmole of shikimic-5-P or 5 μmoles of glutamine (as indicated), + additions in a final volume of 1 ml. Following incubation at 37° for 2 hours aliquots were removed for the assay of anthranilic acid.[12,13]

Substrates and additions	Yield of anthranilic acid, μmoles
Shikimic acid-5-phosphate (1.0 μmole)	0
+ 5.0 μmoles L-aspartic acid	0.10
+ 5.0 μmoles L-glutamic acid	0.20
+ 5.0 μmoles L-glutamine	0.86
+ 5.0 μmoles L-asparagine	0.17
+ 5.0 μmoles NH_4Cl	0.18
L-glutamine (5.0 μmoles)	0
+ 1.0 μmole SA	0
+ 1.0 μmole SA + 1.0 μmole ATP	0.18
+ 1.0 μmole shikimic-5-P	0.80
+ 1.0 μmole Z1	0

(11) The organism was grown for 24 hours with aeration at 30° in minimal medium A (B. D. Davis and E. S. Mingioli, *J. Bact.*, **60**, 17 (1950)) supplemented with 0.2% Difco yeast extract and 0.2% Difco Casamino acids.

(12) A. C. Bratton and E. K. Marshall, *J. Biol. Chem.*, **128**, 537 (1939).

(13) H. W. Eckert, *ibid.*, **148**, 197 (1943).

ably the 5-enolpyruvate of shikimic acid[14,15]), and the two isomers of 6-amino-3,4,5-trihydroxycyclohexane carboxylic acid,[16] could not replace shikimic-5-P.

The formation of anthranilic acid also requires the oxidized form of pyridine nucleotide (DPN^+ or TPN^+). Treatment with charcoal destroys the capacity to form anthranilic acid from shikimic-5-P and L-glutamine. The addition of DPN^+, TPN^+, or DPNH,[17] restores the activity. Furthermore, the addition of DPNase[18] completely abolishes anthranilate formation.[19]

It is a pleasure to acknowledge my indebtedness to Professor J. S. Gots for the mutant strain, and to Professor B. D. Davis for the shikimic-5-P and Z1.

(14) B. D. Davis and E. S. Mingioli, *J. Bact.*, 66, 129 (1953).

(15) C. Gilvarg and B. D. Davis, unpublished observations.

(16) The two isomers were kindly supplied by Professor H. Plieninger, University of Heidelberg.

(17) These extracts contain an active DPNH oxidase.

(18) The Neurospora DPNase was a kind gift of Professor N. O. Kaplan.

(19) Some extracts were found to be inactive unless they were fortified with yeast extract. DPN^+ alone was unable to substitute for the yeast extract, suggesting a possible requirement for another cofactor.

DEPARTMENT OF BIOCHEMISTRY
COLLEGE OF PHYSICIANS AND SURGEONS
COLUMBIA UNIVERSITY P. R. SRINIVASAN
NEW YORK 32, NEW YORK

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BOOK REVIEWS

Annual Reports on the Progress of Chemistry for 1957. Volume LIV. R. S. CAHN, Editor. The Chemical Society, Burlington House, London, W. 1, England. 1958. xx + 445 pp. 14.5 × 22 cm. Price, £2.

The authors of *Annual Reports* face a huge task in their effort to summarize the significant advances in chemistry reported during a year. They acquit themselves of this task very well.

To the specialist within an area the reports provide a perspective to the year's progress which is difficult to achieve from the reading of individual papers. For workers interested in undertaking more intensive study on a topic, the Reports provide an outstanding source of references both to original papers and to recent reviews. For those wishing to survey recent developments in areas outside their own special interests, the Reports serve as an authoritative up-to-date summary which is, for the most part, readable without reference to the original work and without special knowledge in the field.

There are twelve topics in the table of contents which were reviewed last year as well. When, due to space limitations, a topic is covered only after a two or three year accumulation of work, the result is an especially useful review. Such topics in the 1957 Reports and the years since their last appearance are: Radiofrequency Spectroscopy (2), Electrochemistry (3), Thermochemistry (3), and Amino Acids, Peptides and Proteins (2). Other topics appear to be simply summaries of the current status of work and are not restricted to a particular time span. These include: Dielectric Measurements, Stereochemistry, The Mechanism of Enzyme Action Studied with Isotopes, Neuramic Acid, The Biosynthesis of the Purine and Pyrimidine Ring Systems, and the Biosynthesis of Penicillin and Some Other Antibiotics.

The text is adequately, but not abundantly, illustrated with structural formulae. This reviewer particularly appreciated the frequent use of Arabic, rather than the time honored but unwieldy Roman, numerals to refer to the structural formulae. This speeds reading comprehension to a marked degree.

This volume continues the excellent tradition established by the series of *Annual Reports* and is recommended to the attention of every chemist.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALIFORNIA KENNETH CONROW
LOS ANGELES 24, CALIFORNIA

Reaktionmechanismen. Erste Folge. BY VOLKER FRANZEN, Privatdozent an der Universität Heidelberg. Dr. Alfred Hüthig Verlag, Wilckensstrasse 3, Heidelberg, Germany. 1958. 160 pp. 16 × 23.5 cm. Price, DM 18, —.

This book is a collection of papers on reaction mechanisms which appeared in Chemiker-Zeitung, 1955–1957. Titles of the chapters are: Hydride Shifts (Carbinol–Carbonyl Equilibrium, Meerwein–Oppenauer Reduction–Oxidation, Cannizarro Reaction, Quinone Dehydrogenation, Sommelet Reaction, Leuckart–Wallach Reaction, Reduction with Carbonium Ions, Stereochemistry of Hydride Reductions); Electron-deficient Rearrangements (Wolff, Hofmann, Lossen, Curtius, Schmidt and Baeyer–Villiger Rearrangements and Ozone Cleavage); Carbonyl Reactions (Addition Reactions, Aldol, Perkin and Grignard Reactions); Friedel–Crafts Reaction (Alkylation and Acylation); Ester Pyrolysis; Prins Reaction; Wolff–Kishner Reaction; Silver Salt–Bromine Reaction and Decarboxylation. Many of the original papers have been revised and all of the older ones have been brought up to date. The literature is covered through 1956 and in some cases (such as the Grignard equilibrium), where particu-