PROCEEDINGS OF THE BIOCHEMICAL SOCIETY

The 493rd Meeting of the Society was held at the University of Liverpool on Tuesday–Friday, 15–18 April 1969, when the following papers were presented:

SYMPOSIUM ON 'NATURAL SUBSTANCES FORMED BIOLOGICALLY FROM MEVALONIC ACID'

Chemistry of Mevalonic Acid

By J. W. CORNFORTH and R. H. CORNFORTH.
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Mevalonic acid (I) has become a key intermediate in isoprenoid biosynthesis since its discovery in 1956. Among its advantages are the following.

(1) It does not seem to be utilized in metabolic processes for anything except isoprenoid synthesis.

(2) It is water-soluble and can penetrate to the site of synthesis in many (though not all) living tissues.

(3) It is relatively easy to synthesize, and ^{14}C -labelled preparations were available very soon after its discovery.

In the course of investigating the biosynthesis of isoprenoids, and the mechanism of individual enzymic steps in this natural process, our group has had occasion to synthesize fourteen distinct varieties of labelled mevalonic acid and to use all of them to answer specific questions presented by the research. In addition, both the 'natural' and the 'unnatural' enantiomers of mevalonic acid have been synthesized. Several of the labelled mevalonic acids made available by these chemical syntheses have proved useful beyond the range of the experiments for which they were initially devised.

The biosynthetic experiments have usually dictated the nature of the label to be used, as well as its position in the precursor. The interplay of chemistry with biochemical requirements is illustrated in several of the examples discussed.

As a dihydroxyisovaleric acid, mevalonic acid would not be expected to exhibit any unusual chemical properties, and it has never been studied for its chemical behaviour alone. Nevertheless, there is at least one unsolved mystery surrounding the chemistry of mevalonic acid derivatives: the

observed acid-catalysed exchange of oxygen at position 3 with the oxygen of aqueous media. In addition, one synthesis of the acid has revealed an unsuspected exchange of hydrogen in borohydride anions.

Conversion of Mevalonic Acid into Terpene Hydrocarbons

By G. POPJÁK. (*Department of Biological Chemistry, University of California School of Medicine, Los Angeles, California, U.S.A.*)

On the Enzymes Catalysing the Transformation of Squalene to Lanosterol

By S. YAMAMOTO and K. BLOCH. (*The James Bryant Conant Laboratory, Departments of Chemistry and of Biochemistry and Molecular Biology, Harvard University, Cambridge, Mass. 02138, U.S.A.*)

The oxidative cyclization of squalene to lanosterol has been the subject of both chemical and enzymic studies by a number of investigators. Recently the intermediacy of chemically synthesized 2,3-oxidosqualene (Van Tamelen & Curphey, 1962) in the squalene–lanosterol conversion was established in two laboratories (Corey, Russey & Ortiz de Montellano, 1966; Van Tamelen, Willet, Clayton & Lord, 1966). These findings have received further support by the isolation and partial purification of a microsomal enzyme that catalyses the cyclization of 2,3-oxidosqualene to lanosterol (Dean, Ortiz de Montellano, Bloch & Corey, 1967). This reaction does not require oxygen or NADPH.

2,3-Oxidosqualene sterol cyclase has been solubilized from hog liver microsomes with the aid of sodium deoxycholate (Dean *et al.* 1967). After numerous futile attempts to purify the solubilized enzyme further, it was found that high concentrations of salt are required for maximal enzyme activity. The effect of salt on enzyme activity has been partially clarified by the results of gel filtration on Sephadex G-200. When the Sephadex column was equilibrated and eluted with KCl (0.4M) in