a large number of quinones are capable of restoring oxidation, they do not restore this activity by the same respiratory sequence as does the natural quinone. By the use of respiratory inhibitors or by following the reduction of the respiratory carriers spectrophotometrically, it has been possible to show that many of the quinones that restore only oxidation fail to utilize the major respiratory chain but instead by-pass completely or bridge a section of the respiratory chain. Since quinones may accept electrons from one segment of the respiratory chain, by-pass other respiratory carriers and re-enter the terminal position of the major chain, it is possible to determine sites of phosphorylation within the segments that have not been by-passed. In this manner it has been possible to demonstrate phosphorylative sites in the span between NAD⁺ and quinone, between quinone and cytochrome *b* and between cytochrome *c* and oxygen.

Studies with the quinone-depleted system have indicated that the quinones may be directly involved in the phosphorylative events. Incubation of the quinone-depleted system with vitamin K₁, inorganic phosphate containing ³²P, and an electron donor resulted in the formation of a lipid-extractable quinone that was distinct from vitamin K₁ and dihydrovitamin K after chromatography. Of interest was the finding that the enzymically formed compound co-migrated with the synthetic chromanyl phosphate derivative of vitamin K₁. The enzymically formed compound appeared to be derived from vitamin K₁, since it was found to contain ¹⁴C in experiments in which the starting quinone was ¹⁴C-labelled vitamin K₁. The u.v. and i.r. spectra and chromatographic properties of the enzymically formed compound were found to be compatible with a phosphorylated derivative of reduced vitamin K. Although the enzymically formed compound is unstable, a stable addition complex can be formed with mercaptoethanol. This stable complex may permit chemical characterization of the quinol derivative.

It has been possible to obtain some information about the role of quinones in oxidative metabolism. However, it has been shown that bacteria contain a large number of different types of quinones. For example, *M. phlei* contains MK₉(II-H) and MK₈(II-H). Other micro-organisms may contain both benzo- and naphtha-quinones, a series of one type of quinone differing in side chain length (C₄-C₁₀), or differing in the number of saturated isoprenoid units in the side chain. Any analysis of the role of quinones in oxidative metabolism must take into account the possible function of the numerous quinones found in one system. These compounds may represent residual products of quinone biosynthesis or degradation or may play a more subtle metabolic role.

Terpenoids in Insects

By PETER KARLSON. (*Institut für Physiologische Chemie der Philipps-Universität, Marburg/Lahn, Germany*)

This review deals with the occurrence and function in insects of various compounds that are presumably derived from mevalonic acid. The biochemical pathways of their biogenesis are largely unknown.

Sterols and steroid hormones. It is well known that insects are unable to synthesize cholesterol or other sterols from mevalonate. Sterols are essential nutritional factors. However, insects are able to convert cholesterol into ecdysone and 20-hydroxyecdysone. The biochemistry of these 'moulting hormones' will be reviewed briefly. Recent work in my laboratory has led to the preliminary characterization of an enzyme system that converts ecdysone into two metabolites that are biologically inactive.

Juvenile hormones. Two naturally occurring juvenile hormones have been identified. They differ from methyl 10,11-epoxyfarnesoate in having one or two ethyl groups instead of the usual methyl groups. Several C₁₅ terpenoids from plants, e.g. juvabione, have considerable juvenile-hormone activity. The same is true for derivatives of farnesol and for synthetic substances structurally related to juvabione.

Pheromones and defence substances. Pheromones are secretions that serve as 'chemical messengers' among individuals of the same species. Among these, we find some terpenoid alcohols and aldehydes (e.g. geraniol, citronellal). The biology of these compounds will be reviewed. Even larger is the spectrum of the defence substances. Remarkably, cortexone and other corticosteroids serve as defence substances for some aquatic beetles. Ants produce a wide variety of defence substances, which are mostly related to terpenoids, e.g. dendrolasin and iridomyrmecin, a lactone possessing antibiotic and insecticidal properties.

Biosynthesis of Terpenoid Alkaloids

By A. R. BATTERSBY. (*Department of Organic Chemistry, University of Liverpool*)

Both the fungi and the higher plants form natural products in which nitrogen has been built into a skeleton which, by its structure, is apparently terpenoid in origin or at least partly so. Examples are the alkaloids of ergot, the diterpene bases present in many *Aconitum* species, the simple pyridine and piperidine alkaloids from *Skytanthus* and so on. Undoubtedly the largest group of nitrogenous terpenes, however, is that containing

the indole alkaloids of higher plants. The number of these indole alkaloids known has increased rapidly over the last few years, and over 600 are now known. A tryptamine residue appears almost invariably and, in the few cases examined by tracer methods, this residue has been found to be derived in the expected way from tryptophan. The remaining nine or ten skeletal carbon atoms appear in what at first sight seems a bewildering variety of different arrangements, but closer inspection allows three main groups to be discerned. The paper will be concerned first with the terpenoid origin of these three non-tryptamine units and secondly with the way in which the tryptamine portion of the final products is built on to the terpenoid portion. In each of these sections two important phases are

apparent. The initial phase involves determination of those substances that are used as the building blocks. With this achieved, the second phase can be initiated; here the intermediates on the pathway are identified and this in turn leads to a study of the mechanism of each step in the biosynthetic sequence. At present a most exciting stage has been reached where hypothesis, tracer experiment, structure determination, and isolation work can be combined in a very powerful way. All these aspects will be illustrated. Extensive use is made of ^{14}C labelling in the initial phase and of multiple labelling with ^3H and ^{14}C in the second phase. The substances used in this work include mevalonate, geraniol, merol, linalool, loganin, secologanin, vincoside and, of course, the indole alkaloids.

COMMUNICATIONS

Studies on the Relationship Between Molecular Structure and the Biliary Excretion of Organic Compounds

By P. C. HIROM, P. MILLBURN, R. L. SMITH and R. T. WILLIAMS. (*Department of Biochemistry, St Mary's Hospital Medical School, London W.2*)

A diversity of organic compounds are excreted in the bile (Smith, 1966). Molecular weight and polarity are important factors in determining the extent to which a compound undergoes biliary elimination (Abou-El-Makarem, Millburn, Smith & Williams, 1967*a,b*; Millburn, Smith & Williams, 1967*a,b*). However, although certain structural features of a molecule probably influence its biliary excretion (Ryan & Wright, 1962; Williams, Millburn & Smith, 1965; Smith & Williams, 1966; Hearse, Powell, Olavesen & Dodgson, 1969), the relationship between molecular structure and biliary elimination remains obscure. Therefore, the biliary excretion of about 25 N^4 -acyl sulphonamides of closely related structures was examined. The compounds (100 $\mu\text{moles/kg}$. in 0.2 ml. of dimethyl sulphoxide) were injected intraperitoneally into biliary-cannulated female Wistar albino rats, and the 24 hr. bile was collected and analysed (Millburn *et al.* 1967*b*). They were excreted mainly unchanged in the bile.

The biliary excretion, expressed as a percentage of the dose, of the N^4 -succinyl derivatives of sulphanilamide, sulphacetamide and sulphathiazole (mol.wt. 272, 314 and 355 respectively) was 5, 4 and 54% respectively. The corresponding N^4 -phthalyl derivatives (mol.wt. 319, 362 and 403 respectively) had biliary excretions of 7, 2 and 19%. Thus the presence of a thiazole ring in the N^1 -position of

the above sulphonamides enhances their biliary elimination.

The effect of modifying the N^4 -substituent was investigated with a series of sulphathiazole derivatives. The excretion in the bile of hexahydrophthalyl-, 3-carboxy-2-naphthoyl-, tetrachlorophthalyl- and tetrabromophthalyl-sulphathiazole (mol.wt. 409, 453, 541 and 719 respectively) was about 60% of the dose irrespective of molecular weight. Thus, replacing the benzene ring of the phthalyl portion of phthalylsulphathiazole by a cyclohexane, a naphthalene or a halogenated benzene ring increased biliary excretion threefold.

ω -Carboxyacylsulphathiazoles containing as the N^4 group $\text{HO}_2\text{C}\cdot[\text{CH}_2]_n\cdot\text{CO}-$ with $n=0-8$ (mol.wt. 327-439) were also studied. When $n=0$ or 1, the biliary excretion was 15-20% of the dose; when $n=2$ or 4-8, the excretion was 40-50%; but when $n=3$, the high value of 74% was obtained.

These results support the hypothesis that polar molecules with molecular weights of at least 325 ± 50 are excreted in the bile of rats to the extent of 10% or more of the dose (Millburn *et al.* 1967*a*). However, above the minimum requirement there appears to be no close correlation between molecular weight and extent of biliary excretion in this series of compounds. These experiments also show that modifying the structure of a molecule can markedly alter its affinity for hepatobiliary elimination. The results will be further discussed in relation to molecular structure and physicochemical properties.

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Abou-El-Makarem, M. M., Millburn, P., Smith, R. L. & Williams, R. T. (1967*a*). *Biochem. J.* 105, 1269.