cluded a consideration of some recent controversies on the action of cytochalasin B on microfilaments, and on the role of microtubules in chromosome movement. The small size of this meeting provided an opportunity for the informal discussion of current developments by all the participants and, in the opinion of the writer, such conferences can contribute much to clarifying—if not resolving—conflicting points of view.

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Arene Oxides: Biochemistry and Metabolism

Although arene oxides (epoxides of aromatic compounds) were proposed as reactive intermediates in the metabolism of polycyclic aromatic compounds some 25 years ago by E. Boyland, the first symposium on this subject was held at the Roche Institute of Molecular Biology, Nutley, New Jersey, on 6 and 7 April 1972. Arene oxides have become the focal point of interest in laboratories around the world because of the possibility of obtaining them synthetically in sufficient amounts for studying their chemical, physical, and biological properties. It has become possible to demonstrate that they are in fact the primary oxidation products of catalytically hydroxylated—for example by aryl hydroxylase (cytochrome P-450)—aromatic compounds. Naphthalene and dibenz(*a,h*)anthracene (directly) and brombenzene and benzo(*a*)pyrene (indirectly) yield the corresponding arene oxides as primary oxidation products on treatment with cytochrome P-450. The oxides are highly reactive electrophiles with a lifetime of minutes under physiological conditions. They rearrange to phenols, which react with glutathione to yield adducts that are then converted to mercapturic acid. With a water molecule arene oxides give rise to corresponding dihydrodiols. The rearrangement and hydration are presumably catalyzed by enzymes.

Of special interest is the cytotoxicity of arene oxides resulting from covalent binding to proteins and nucleic acids. Direct evidence was presented relating cytochrome P-450–catalyzed arene oxide formation to cytotoxicity, mutagenicity, and carcinogenicity of

compounds such as naphthalene, benzo(*a*)pyrene, 7,12-dimethylbenz(*a*)anthracene, K-region oxides of several carcinogenic hydrocarbons of the benz(*a*)anthracene series, and phenanthrene. The evidence of cytotoxicity of halogenated benzene derivatives and 2-allyl-2-isopropylacetamide, due to the same metabolic pathway, was also presented. Data in the above experiments have been obtained from cells in tissue culture as well as from intact, experimental animals.

A rapid assay method for benzo(*a*)-pyrene hydroxylase activity was described. During the development of the assay, data were obtained on products of interaction of arene oxides with proteins and nucleic acids; these products are being characterized.

The studies reported at the symposium demonstrated the importance of understanding the toxicity of chemical compounds at the molecular level. Recent advances have already led to suggestions for protection against chemical toxicity. This could be achieved by the use of cytochrome P-450 inhibitors or with drugs that react preferentially with arene oxides and act as scavengers. A rational approach to new drugs design would be to develop molecules that cannot be converted to arene oxides in the presence of the aryl hydroxylases cytochrome P-450 or P-448.

About 50 investigators participated in the Symposium. Those who presented contributions to the field discussed at the Symposium, or acted as chairmen of the sessions, were E. Boyland (University of London), B. B. Brodie (NIH), J. W. Daly (NIH), F. DeMatteis (Medical Research Council, Great Britain), H. V. Gelboin (NIH), J. R. Gillette (NIH), T. Hayakawa (Roche Institute of Molecular Biology), C. Heidelberger (University of Wisconsin), D. M. Jerina (NIH), W. Levin (Hoffmann-La Roche Inc.), P. Sims (Chester Beatty Research Institute, Great Britain), S. Udenfriend (Roche Institute of Molecular Biology), L. W. Wattenberg (University of Minnesota), and B. Witkop (NIH). Many others participated in discussions.

The Roche Institute of Molecular Biology has published a collection of abstracts of the symposium papers supplemented with an up-to-date bibilography of research in the field of arene oxides.

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