FUSED PYRIMIDINES

Edited by

D. J. Brown

Part II

PURINES

J. H. Lister

Chester Beatty Research Institute,
Institute of Cancer Research,
London

With contributed essays on spectra by

R. L. JONES and P. D. LAWLEY
Chester Beatty Research Institute

and collaboration in part by

G. H. HITCHINGS and G. B. ELION
Wellcome Research Laboratories, Tuckahoe,

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The Chemistry of Heterocyclic Compounds

The chemistry of heterocyclic compounds is one of the most complex branches of organic chemistry. It is equally interesting for its theoretical implications, for the diversity of its synthetic procedures, and for the physiological and industrial significance of heterocyclic compounds.

A field of such importance and intrinsic difficulty should be made as readily accessible as possible, and the lack of a modern detailed and comprehensive presentation of heterocyclic chemistry is therefore keenly felt. It is the intention of the present series to fill this gap by expert presentations of the various branches of heterocyclic chemistry. The subdivisions have been designed to cover the field in its entirety by monographs which reflect the importance and the interrelations of the various compounds, and accommodate the specific interests of the authors.

In order to continue to make heterocyclic chemistry "as readily accessible as possible", new editions are planned for those areas where the respective volumes in the first edition have become obsolete by overwhelming progress. If, however, the changes are not too great so that the first editions can be brought up-to-date by supplementary volumes, supplements to the respective volumes will be published in the first edition.

Research Laboratories
Eastman Kodak Company
Rochester, New York

ARNOLD WEISSBERGER

Princeton University
Princeton, New Jersey

EDWARD C. TAYLOR

Foreword to The Fused Pyrimidines

Originally it was intended to present all the fused pyrimidine systems in one volume of this series. Resurgence of interest in purines and quinazolines, the development of pteridine chemistry, and the wide exploration of a great many new fused systems embracing the pyrimidine ring, have made the task impossible.

The fused pyrimidines will now be covered in four parts, of which Dr. Armarego's *Quinazolines* was the first and Dr. Lister's *Purines* is the second. Two others, dealing with *Pteridines* and *Miscellaneous Fused Pyrimidines* respectively, are in active preparation. Eventually, this bracket of volumes will bring to the series the expertise of four senior authors and several coauthors with wide and diverse experience in the field.

It is a privilege to assist Dr. Weissberger, Dr. Taylor, and the authors in organizing this project and in maintaining a measure of uniformity and balance in its parts.

D. J. BROWN

The Australian National University
Canberra, Australia

EDWARD C. TAYLOR

Department of Chemistry
Princeton University
Princeton, New Jersey

Preface

This book, which forms part of the series devoted to Fused Pyrimidines, follows, insofar as subject matter permits, the format adopted in *The Pyrimidines*, the parent member of the series. As in previous volumes a critical approach to the subject is taken—treating theoretical aspects of the chemistry in outline and giving the major emphasis to practical aspects, which are supported by the appendix tables. The tables furnish melting points and selected source references for simple purine derivatives known up to the end of 1969. The literature has been surveyed in detail from Scheele's isolation of uric acid in 1776 to December 1969 with additional coverage of the leading journals to late 1970. As nucleoside forms are outside the terms of reference, these are only mentioned in the text where some interesting feature or reaction of the purine moiety is involved or to draw attention to some notable difference in behaviour between the latter and the free purine.

Purine chemistry as we know it today had its origins in Fischer's prodigous work, started nearly ninety years ago, in which the synthesis of all the naturally occurring purines then known was accomplished. This fruitful period, associated also with names such as Traube, Biltz, Gabriel, and Johns, was followed by a decline in interest in the chemistry of these nitrogenous bases which lasted for nearly four decades. In the early 1950's, however, following upon the determination of partial structures of the nucleic acids, a new period of expansion was initiated. This arose from the realisation that man-made purines and purine analogues could possibly interfere with nucleic acid biosynthesis and therefore act as growth inhibitors. Although many hundreds of purines have been prepared with this end in view, the results have been disappointing and only derivatives of 6-mercaptopurine have found any wide clinical application in this field of chemotherapy.

For help in the preparation of this work I am indebted to a number of colleagues and others who have contributed in various ways. Drs. G. H. Hitchings and G. B. Elion very kindly gave me access to an unpublished survey they had made of the early purine chemistry. My thanks are also due to my co-authors, Drs. R. L. Jones and P. D. Lawley

for their informative essays on infrared and ultraviolet spectra, respectively. Colleagues who have sent me their results before publication and who, in so doing, have helped to reduce the "outdatedness" of the volume at the time of publication, include Professor Adrian Albert, Drs. G. B. Brown, A. Giner-Sorolla, R. Hull, Paul T'so, and T. L. V. Ulbricht.

I have also been greatly helped by the facilities afforded me at the Chester Beatty Research Institute and for these I wish to express my deep gratitude to the recently retired director, Sir Alexander Haddow, F.R.S. Among the people directly concerned have been Michael Docherty and other members of the Photographic Department, and the Library staff, who at all times have provided an efficient and willing service. It would be remiss of me, however, not to record a special word of praise for the Herculean efforts of Miss Margaret Foster and Mrs. Audrey Inglefield, who between them have carried out the arduous task of typing both the draft and final stages with great cheerfulness. My sincere thanks also are accorded to my editor and former colleague, Dr. D. J. Brown, for his guidance and encouragement, and last but by no means least to my wife for her constant support and for patiently enduring the trials of having an author in the family.

J. H. LISTER

Chester Beatty Research Institute,
Institute of Cancer Research: Royal Cancer Hospital,
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