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978-0-521-10589-7 - The Chemistry and Biology of Benz[a]Anthracenes

M. S. Newman, B. Tierney and S. Veeraraghavan

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*Cambridge Monographs on Cancer Research*

The chemistry and biology of benz[a]anthracenes

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THE CHEMISTRY AND BIOLOGY OF

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**BENZ[A]ANTHRACENES**

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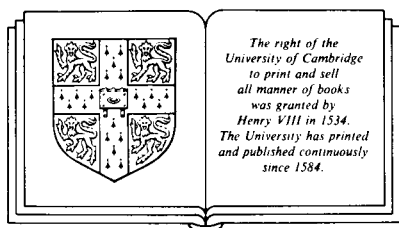
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## Authors' preface

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In Part 1 of this book the syntheses of benz[a]anthracenes are covered from the middle 1930s to the end of 1984. Prior to the middle 1930s almost all of the references are to quinones of possible use as dyestuff intermediates and are not covered here. Early syntheses were reviewed by Cook (1931). The synthetic procedures of interest in early studies of the carcinogenic activity of polycyclic aromatic hydrocarbons were reviewed by Fieser (1937). The present state of the synthetic approaches to benz[a]anthracenes is organized into several different categories. Advantages and difficulties in various synthetic routes are pointed out. Often the poor yields in certain steps should be capable of improvement by the use of alternate reagents and methods. Since many of the older methods have not been restudied, it is left to the reader to decide the best course of action in any chosen case.

The syntheses of arene oxides, dihydrodiols, quinones, phenols and diphenols in the benz[a]anthracene series will not be covered in depth and the reader is referred to the monograph *Polycyclic Hydrocarbons and Carcinogenesis* by Harvey (1985), which addresses these topics more fully.

In Part 2 the biological properties of benz[a]anthracene and its substituted derivatives (such as the highly active 7,12-dimethylbenz[a]anthracene) are discussed in relation to literature available up to the end of 1985. These types of compounds can be formed during the combustion of organic matter (such as coal or tobacco) and are widely distributed throughout the environment; being present in the air, in water and in the soil. Because of their occurrence in the environment and because certain benz[a]anthracene derivatives exhibit potent biological activity they have been the subject of intense study.

The text in Part 2 has been divided into four sections: metabolism,



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interactions with cellular macromolecules, mutagenicity and carcinogenicity. A brief, general, historical perspective has been given at the beginning of the metabolism section. I have tried to provide enough background information in each section so that the development and significance of ideas can be followed. Review articles have been cited wherever possible.

B.T. wishes to thank members of the Cancer Research Unit, York, for their understanding whilst this work was being prepared and his wife without whose support and encouragement this work would not have been possible.

M.S.N.

B.T.

S.V.

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## Abbreviations employed in this book

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**Journal titles**

- Acta Crystallogr.* Acta Crystallographica  
*Acta Unio Int. Cancrum* Acta Unio Internationalis contra Cancrum  
*Adv. Lipid Res.* Advances in Lipid Research  
*Am. J. Cancer* American Journal of Cancer  
*Am. J. Physiol.* American Journal of Physiology  
*An. Assoc. Quim, Argent.* Anales de la Asociacion Quimica Argentina  
*Angew. Chem.* Angewandte Chemie  
*Ann. Chim. App. Akad. Nauk SSSR* Annalen Chemie Applicata Akad. Nauk. SSSR  
*Annalen* Justus Liebig's Annalen der Chemie  
*Arch. Biochem. Biophys.* Archives of Biochemistry and Biophysics  
*Arch. Geschwulstforsch.* Archiv für Geselwulstforschung  
*Aust. J. Chem.* Australian Journal of Chemistry  
*Ber.* Berichte der Deutschen Chemischen Gesellschaft  
*Biochem. J.* Biochemical Journal  
*Biochem. Pharmacol.* Biochemical Pharmacology  
*Biochim. Biophys. Acta* Biochimica et Biophysica Acta  
*Biomed. Mass Spectrum.* Biomedical Mass Spectrometry  
*Br. J. Cancer* British Journal of Cancer  
*Br. Med. J.* British Medical Journal  
*Bull. Acad. Polon. Sci., Sér. Sci. Chim.* Bulletin de l'Academie Polonaise de Sciences, Série des Sciences Chimique  
*Bull. Chem. Soc. Japan* Bulletin of the Chemical Society of Japan  
*Bull. Int. Acad. Polonaise* Bulletin International de l'Académie des Sciences  
*Bull. Soc. Chem. Japan* Bulletin of the Society for Chemistry Japan  
*Bull. Soc. Chim. Belges* Bulletin des Sociétés Chimiques Belges  
*Bull. Soc. Chim. France* Bulletin de la Société Chimique de France  
*Cancer Biochem. Biophys.* Cancer Biochemistry and Biophysics  
*Cancer Lett.* Cancer Letters  
*Cancer Res.* Cancer Research  
*Can. J. Chem.* Canadian Journal of Chemistry  
*Can. J. Res.* Canadian Journal of Research  
*Chem. Abst.* Chemical Abstracts  
*Chem. Ber.* Chemische Berichte  
*Chem. Biol. Interact.* Chemistry and Biological Interactions  
*Chem. Ind. (London)* Chemistry and Industry (London)

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- Chem. Lett. Chem. Soc. Japan* Chemistry Letters, The Chemical Society of Japan  
*Chi. Dai. Kog. Ken. Hok.* Chiba Daigaku Kogakubu Kenkyu Hokoku  
*Collect. Czech Chem. Commun.* Collection of Czech Chemical Communications  
*C. R. Acad. Sci. URSS* Comptes rendus de l'Académie des Sciences, URSS  
*C. R. Hebd. Séances Acad. Sci.* Comptes rendus Hebdomadaires des Séances de l'Académie des Sciences  
*C. R. Hebd. Séances Acad. Sci. Sér. C* Comptes rendus Hebdomadaires des Séances de l'Académie des Sciences, Séries C, Séries Chimiques  
*Curr. Sci.* Current Science  
*Dokl. Akad. Nauk. SSSR* Doklady Akademii Nauk SSSR  
*Dokl. Bolg. Acad. Nauk* Doklady Bolgarshoi Akademii Nauk  
*Drug Met. Dispos.* Drug Metabolism and Disposal  
*Edinburgh Med. J.* Edinburgh Medical Journal  
*FEBS Lett.* Federation of European Biochemical Societies Letters  
*Fed. Proc.* Federation of American Societies for Experimental Biology Proceedings  
*Gazz. Chim. Ital.* Gazzetta Chimica Italiana  
*Geochim. Cosmochim. Acta* Geochimica et Cosmochimica Acta  
*Helv. Chim. Acta* Helvetica Chimica Acta  
*Heterocycles* Heterocycles  
*Indian J. Chem.* Indian Journal of Chemistry  
*Indian J. Phys.* Indian Journal of Physics.  
*Industr. Engng Chem.* Industrial and Engineering Chemistry  
*Int. Abst. Surg.* International Abstracts of Surgery  
*Int. J. Cancer* International Journal of Cancer  
*Izv. Akad. Nauk SSSR Otdel. Khim. Nauk.* Izvestiya Akademii Nauk SSSR Otdelenii Khimicheskikh Nauk  
*J. Am. Chem. Soc.* Journal of the American Chemical Society  
*J. Am. Med. Assoc.* Journal of the American Medical Association  
*J. Biol. Chem.* Journal of Biological Chemistry  
*J. Chem. Engng Data* Journal of Chemical and Engineering Data  
*J. Chem. Phys.* Journal of Chemical Physics  
*J. Chem. Res.* Journal of Chemical Research  
*J. Chem. Soc.* Journal of the Chemical Society  
*J. Chem. Soc., Chem. Commun.* Journal of the Chemical Society, Chemical Communications  
*J. Chem. Soc. Japan* Journal of the Chemical Society of Japan  
*J. Chem. Soc., Perkin Trans. I* Journal of the Chemical Society, Perkin Transactions I  
*J. Exp. Med.* Journal of Experimental Medicine  
*J. Gen. Chem. (USSR)* Journal of General Chemistry, USSR  
*J. Heterocyclic Chem.* Journal of Heterocyclic Chemistry  
*J. Indian Chem. Soc.* Journal of the Indian Chemical Society  
*J. Labelled Compd. Radiopharm.* Journal of Labelled Compounds and Radiopharmaceuticals  
*J. Math. Sci.* Journal of Mathematical Science  
*J. Med. Chem.* Journal of Medicinal Chemistry  
*J. Nat. Cancer Inst.* Journal of the National Cancer Institute  
*J. Org. Chem.* Journal of Organic Chemistry  
*J. Soc. Org. Syn. Chem., Japan* Journal of the Society of Organic Synthetic Chemistry, Japan  
*J. Prakt. Chem.* Journal für Praktische Chemie  
*J. Path. Bact.* Journal of Pathology and Bacteriology  
*Liebig's Annal. Chem.* Justus Liebig's Annalen der Chemie

*Abbreviations employed*

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- Mitt. Geb. Lebensmittelunter. Hyg.* Mitteilungen aus dem Gebeite der Lebensmittel-  
 untersuchung und Hygiene  
*Monatsh. Chem.* Monatshefte für Chemie  
*Mutation Res.* Mutation Research  
*Nippon Kag. Kaishi* Nippon Kagaku Kaishi (Continuation of Journal of the Chemical  
 Society of Japan)  
*Nucleic Acids Res.* Nucleic Acids Research  
*Org. Prep. Proc. Int.* Organic Preparations and Procedures International  
*Proc. Am. Pet. Inst.* Proceedings, American Petroleum Institute  
*Proc. Nat. Acad. Sci. USA* Proceedings of the National Academy of Sciences of the  
 United States of America  
*Proc. Nat. Cancer Inst.* Proceedings of the National Cancer Institute  
*Proc. R. Soc. (London), A* Proceedings of the Royal Society of London, Series A  
*Proc. Soc. Exp. Biol. Med.* Proceedings of the Society for Experimental Biology and  
 Medicine  
*Prog. Exp. Tumor Res.* Progress in Experimental Tumor Research  
*Rec. Trav. Chim.* Recueil des Travaux Chimiques des Pays-Bas  
*Recerca Sci. Recerca Science*  
*Roczniki Chem.* Roczniki Chemii  
*Science* Science (Washington, DC)  
*Science Cult.* Science and Culture  
*Synthesis* Synthesis  
*Synthetic Commun.* Synthetic Communications  
*Tetrahedron* Tetrahedron  
*Tetrahedron Lett.* Tetrahedron Letters  
*Trans. Faraday Soc.* Transactions of the Faraday Society  
*Yale J. Biol. Med.* Yale Journal of Biology & Medicine  
*Z. Ernaehungswiss.* Zeitschrift für Ernaehungswissenschaft  
*Z. Krebsforsch.* Zeitschrift für Krebsforschung  
*Z. Kristallogr.* Zeitschrift für Kristallographie  
*Z. Naturforsch.* Zeitschrift für Naturforschung  
*Z. Physiol. Chem.* Zeitschrift für Physiologische Chemie  
*Zh. Obshch. Khim.* Zhurnal Obshchei Khimii

**Other abbreviations**

- BA benz[a]anthracene  
 BAQ benzanthracene quinone (7,12-benz[a]anthraquinone)  
 DHBA dihydrobenz[a]anthracene  
 DMBA dimethylbenz[a]anthracene  
 EBA ethylbenz[a]anthracene  
 HOBA (OHBA) hydroxybenz[a]anthracene  
 MBA methylbenz[a]anthracene  
 PBA propylbenz[a]anthracene  
 i-PBA isopropylbenz[a]anthracene  
 TMBA trimethylbenz[a]anthracene  
 BrBA, ClBA, FBA halogenated benz[a]anthracene with Br, Cl or F, respectively  
 MeOBA, CH<sub>3</sub>OBA methoxybenz[a]anthracene  
 PhBA phenylbenz[a]anthracene  
 TeMBA tetramethylbenz[a]anthracene  
 BA1,2-dihydrodiol *trans*-1,2-dihydro-1,2-dihydroxybenz[a]anthracene  
 BA1,2,-diol 3,4-epoxide 1,2-dihydro-1,2-dihydroxy-3,4-epoxybenz[a]anthracene  
 OHMBA hydroxymethylbenz[a]anthracene  
 3-MC 3-methylcholanthrene

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7-OHM-12-MBA    7-hydroxymethyl-12-methylbenz[a]anthracene

7,12-DiOH-DMBA    7,12-dihydroxymethylbenz[a]anthracene

*m*-CPBA    *m*-chloroperoxybenzoic acid

B[a]P    benzo[a]pyrene

B[e]P    benzo[e]pyrene

NADPH    nicotinamide-adenine dinucleotide phosphate, reduced

PAH    polycyclic aromatic hydrocarbon

PB    phenobarbital

poly(A)    polyadenylic acid

poly(G)    polyguanylic acid

TCDD    2,3,7,8-tetrachlorodibenzo-*p*-dioxin

TPA    12-O-tetradecanoylphorbol-13-acetate

HPLC    high-pressure liquid chromatography

tlc    thin-layer chromatography