The Determination of Molecular Structure

Structure Elucidation of Natural Products by Mass Spectrometry. vol. 1, *Alkaloids* (245 pp., $10.50); vol. 2, *Steroids, Terpenoids, Sugars, and Miscellaneous Classes* (316 pp., $10.50). Herbert Budzikiewicz, Carl Djerassi, and Dudley H. Williams. Holden-Day, San Francisco, 1964. Illus.

These books, with the previously published *Interpretation of Mass Organic Compounds*, complete a three-volume compilation of the application of mass spectrometry to the determination of molecular structure. They also cap an amazing 2-year record of publications from the authors' laboratory. Their contributions have been a major factor in the explosive recent growth of this field—the majority of references cited in these books are dated 1963 to 1964.

Natural product structures covered include alkaloids, with iboga, aspidospermine, isoquinoline, colchicine, and lycopodium types; steroids, including alkaloid, ketone, estrogen, and sapogenin types; mono- through triterpenes; long chain derivatives; peptides; carbohydrates; and oxygen heterocyclics. Coverage and treatment is generally thorough and critical. A useful additional chapter is an authoritative summary of techniques for the specific introduction of deuterium into a variety or organic molecules. The authors frequently demonstrate the value of checking mechanisms with such labeling, and this summary should simplify the practice for others. Chemical derivatives that are useful for particular compound classes are also discussed—for example, the ethylene ketal group which can direct the fragmentation of steroids and triterpenes in a predictable manner.

As in *Interpretation of Mass Spectra of Organic Compounds*, detailed mechanisms are proposed for most of the abundant ions in the spectra examined. Despite the lack of full confirmation for many of these, they serve a very useful purpose in that they indicate generalizations and provide guideposts for future work. Some added clarifications are helpful—for example, in volume 2, the use of Shannon's symbol "$\dot{+}$" to designate a radical (odd-electron) ion.

The inclusion of an appendix on the calculation of molecular formulas by high resolution mass spectrometry (this has recently been published in book form) is indicative of the growing awareness of the potential of elemental formula information, although in these volumes only modest use is made of this method, or of computer techniques, for the reduction of data.

In summary, the authors have admirably accomplished their specific objectives, providing a much needed comprehensive reference to mass spectral data on natural products. Perhaps of even more value for the future is the clarification and stimulation provided for further research in the underlying mechanisms of mass spectra. A more thorough understanding and systemization of such mechanisms is necessary to provide a proper framework for the continued explosive expansion of this exciting field.

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Alkylating Agents

Cyclophosphamide (Cytoxan). Proceedings of a symposium (London), October 1963. G. Hamilton Fairley and J. M. Simister, Eds. William and Wilkins, Baltimore, 1965. xii + 200 pp. Illus. $9.75.

Nitrogen mustard and related substances have been under continuing laboratory and clinical investigation since 1946, and they have an established role in the treatment of cancer. Literally hundreds of alkylating agents have been synthesized and at least 50 have been administered to patients with various forms of cancer. The alkylating agents have been investigated for their mechanism of action in vitro and in various biological systems, their chemical reactivity under various conditions, their pharmacological and toxicological effects in animals, and their therapeutic activity in man. Various members of the group have been compared for therapeutic specificity against various forms of cancer in animals and man. The results of the clinical studies indicate that these drugs have a similar spectrum of therapeutic activity. Certain derivatives have distinct advantages—they are effective when given by mouth and only infrequently cause gastrointestinal disturbances.

One of the most intensively studied nitrogen mustard derivatives has been cyclophosphamide (Cytoxan). It differs from the other members of the group in that it is inactive in vitro, but on activation in vivo it produces injury to proliferating normal and neoplastic cells. This book contains the proceedings of a conference on cyclophosphamide, held at the Royal College of Surgeons of England on 4 October 1963. Seventy-four participants described their clinical experiences in using cyclophosphamide to treat cancer. The papers are short, and sometimes only a single case report is presented. The presentations are grouped according to various forms of the disease, but the therapeutic responses are not described in a consistent manner. Little attempt is make to compare the clinical benefits from cyclophosphamide with other alkylating agents. There is a brief section on the use of cyclophosphamide as an immunosuppressive agent. The pharmacology and mechanism of action of cyclophosphamide are not discussed, nor are data presented indicating how it may differ therapeutically from the other alkylating agents.

Cyclophosphamide is a useful agent in the treatment of cancer. It has certain disadvantages in comparison to other alkylating agents. It is more costly and, compared to other available alkylating agents, produces frequent and relatively unique toxicological effects; these include temporary alopecia, which is obviously distressing to female patients, and cystitis which is often hemorrhagic. To its credit, cyclophosphamide can be given intravenously or by mouth, and therapeutic doses appear to produce less platelet depression than the more conventional alkylating agents. It is useful in the treatment of the chronic leukemias, Hodgkin's disease and lymphosarcoma, multiple myeloma, and ovarian, breast, and lung cancers, but its therapeutic spectrum does not appear to differ qualitatively from other active alkylating agents. One exception may be the induction of occasional temporary remissions in acute leukemia in children, but this important observation is not clearly described in the proceedings.

This book is a series of clinical impressions displayed in case reports that are repetitious, and often in-