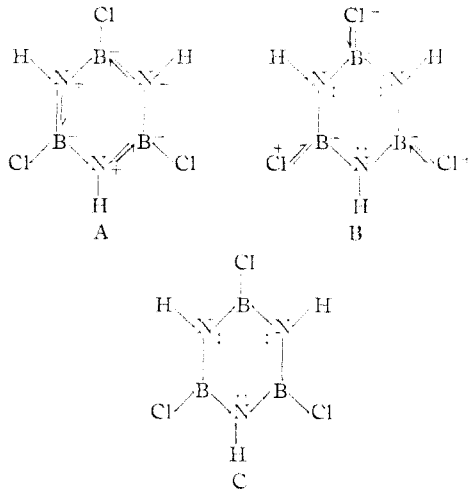


Fig. 1.

mation on the magnitude of this contribution. But the electrical properties of BN[2] and the constancy of the bond length observed in the series BF_3, $BMeF_2$, BMe_2F, BMe_3[5] suggest that the single-bond configuration might be important in some trigonally coördinated boron compounds as well as in the tri-aryls and tri-alkyls.

(5) S. H. Bauer and J. M. Hastings, THIS JOURNAL, **64**, 2686 (1942).

ATOMIC ENERGY RESEARCH ESTAB. R. S. PEASE
HARWELL, BERKS, ENGLAND

RECEIVED JUNE 2, 1952

AN ANTISEROTONIN WHICH IS ORALLY EFFECTIVE

Sir:

Recently, antimetabolites of serotonin have been described which overcome the constriction of segments of arteries elicited by this naturally occurring vasoconstrictor.[1] The suggestion has also been made that such antimetabolites might merit consideration as pharmacological agents capable of influencing favorably some kinds of constriction of vessels seen in higher animals. More recently, it has been found that intravenous administration of 2,3-dimethyl-5-aminoindole will prevent the rise in arterial blood pressure of dogs which follows the intravenous injection of serotinin.

If one envisions a desirable agent for clinical use in a condition such as hypertension, one of the first requisites is that this agent be effective by the oral route. Intravenous adminstration is so objectionable that the need for it would render an otherwise promising substance impractical. When the aminoindoles were given to dogs orally, and the subsequent effect of serotonin on the arterial blood pressure[2] was examined, it was seen that, although the rise in pressure could be inhibited partially, a large dose of analog was required. This was not too surprising since tissues are known to contain enzyme systems which destroy *p*-phenylenediamines, and these analogs are substituted *p*-phenylenediamines. Therefore, an analog of serotonin was sought which would be active by oral administration.

(1) D. W. Woolley and E. Shaw, THIS JOURNAL, **74**, 2948 (1952).
(2) I. H. Page, *J. Pharmacol. and Exp. Therap.*, **105**, 58 (1952).

The corresponding 5-nitroindoles were found to do this, as the following experiment will show. A normal dog was anesthetized with nembutal, and a mercury manometer was connected through a needle to the femoral artery (without surgical operation).[3] The response to intravenous serotonin[4] was noted (Fig. 1). Being thus of proven reactivity, the dog was fed daily 500 mg. of 2-methyl-3-ethyl-5-nitroindole for 4 days, and again challenged with serotonin. The figure will show that even twice the dose of the vasoconstrictor elicited no significant effect. This experiment was repeated in other dogs with similar results.

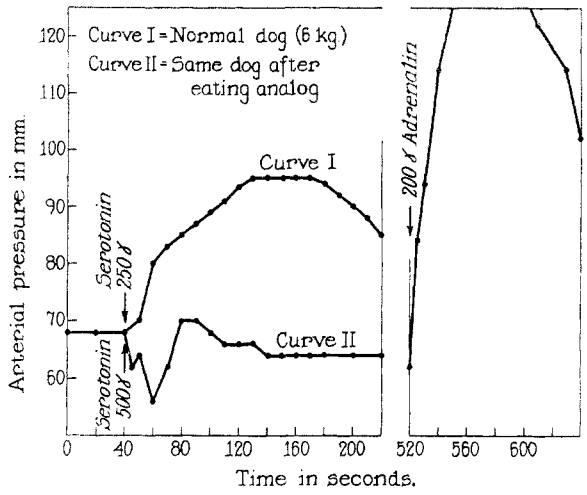


Fig. 1.

This nitroindole was inactive as an antimetabolite of serotonin when tested *in vitro* with artery rings.[1] Its activity *in vivo* suggested that the real antimetabolite, *i.e.*, the aminoindole, was transported in this protected state to the site of action, and there liberated by reduction.

The nitroanalog seemed to be relatively harmless to normal animals. No toxic manifestations have been seen in mice fed it as 1% of their ration. Similarly, dogs fed 500 mg. per day for four days showed no ill effects. Note also in the figure that the normal arterial pressure was not lowered by such feeding.

FROM THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH, NEW YORK D. W. WOOLLEY[5] E. SHAW

RECEIVED JUNE 26, 1952

(3) We are greatly indebted to Dr. I. L. Schwartz for skillfully carrying out these operations.
(4) Serotonin was kindly supplied by the Abbott Laboratories. The weights stated are of serotonin creatinine sulfate.
(5) With the technical assistance of G. Schaffner.

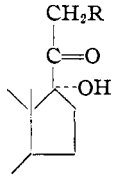
ACYLATION OF 17α-HYDROXY-20-KETOSTEROIDS: COMPOUND L DIACETATE

Sir:

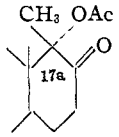
Although acetylation of the C-17 hydroxyl group of 17β-hydroxy-20-ketosteroids can be effected relatively easily with hot acetic anhydride and pyridine,[1] acetylation of the epimeric 17α-hydroxy

(1) C. W. Shoppee and D. A. Prins, *Helv. Chim. Acta*, **26**, 185 (1943); J. von Euw and T. Reichstein, *ibid.*, **30**, 205 (1947).

derivatives (I), of which the naturally occurring adrenal cortical steroids are the most common examples, has not hitherto been accomplished.

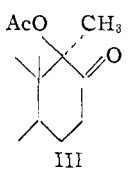


I

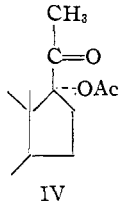


II

Thus allopregnane-3β,17α-diol-20-one (Reichstein's compound L) with acetic anhydride and pyridine furnishes only a 3-monoacetate, whereas treatment of the ketol with BF_3–HOAc–Ac_2O results in rearrangement[2] and the formation of 17a-methyl-D-homoandrostane-3β,17aα-diol-17-one diacetate (II) in virtually quantitative yield.[3] The reaction of compound L with acetic anhydride and acetic acid in the presence of *p*-toluenesulfonic acid, on the other hand, follows a different course. Under these conditions a diacetyl derivative, m.p. 197.5–198.5°, $[\alpha]_D$ −9.3° (dioxane), found: C, 71.72; H, 9.08, is obtained, which differs from both epimeric D-homo derivatives II and III,[2] and from which compound L can be regenerated by *mild* alkaline hydrolysis. On the basis of this evidence and the infrared spectrum (maxima at 1715 and 1735 cm.$^{-1}$), the new product is formulated as allopregnane-3β,17α-diol-20-one diacetate (IV) (L diacetate). It has further been shown that treatment of allopregnane-3β,17β-diol-20-one (iso L) with *p*-toluenesulfonic acid, acetic acid, and acetic anhydride affords the known iso L diacetate.[1]



III



IV

This reaction provides a method for protecting sensitive ketol side chains of adrenal steroids from attack by reagents that might otherwise promote degradation or rearrangement.

DEPARTMENT OF CHEMISTRY
THE RICE INSTITUTE RICHARD B. TURNER
HOUSTON 1, TEXAS

RECEIVED JULY 23, 1952

(2) *Cf.* C. W. Shoppee and D. A. Prins, *Helv. Chim. Acta*, **26**, 201 (1943).

(3) R. B. Turner, forthcoming publication.

BOOK REVIEWS

Punched Cards. Their Applications to Science and Industry. Edited by ROBERT S. CASEY, W. A. Sheaffer Pen Co., Fort Madison, Iowa, and JAMES W. PERRY, Massachusetts Institute of Technology, Cambridge, Massachusetts. Reinhold Publishing Corporation, 330 West 42nd Street, New York 18, N. Y. 1951. viii + 506 pp. 16.5 × 23.5 cm. Price, $10.00.

The primary purpose of this book is to furnish sufficient information to permit the application of punched card techniques to individual problems although the editors admit that the present state of knowledge of this subject does not allow full definitive treatment. Another purpose is to record present knowledge and experience so that better use of the presently available punched card devices and design of devices better suited to practical needs will be stimulated. Hand-sorted edge-punched cards are discussed in greater detail than machine-sorted cards; in fact, the book is intended to serve as an operating instruction manual for edge-punched cards. The discussions concerned with the use of machine-sorted cards indicate that the capabilities of available machines are not being fully exploited, *e.g.*, the automatic reproduction of replicates of original punched cards. Also, the advantages of pre-filing of machine-sorted punched cards for hand selection are not adequately discussed.

The book is divided into five parts. Part 1 is concerned with punched card fundamentals such as elementary manipulations of hand-sorted cards, the application of a simple coding procedure to the assembly of information on the chemistry of coal formation and to brief descriptions of commercially available hand-sorted and mechanical punched card systems, equipment and supplies. It was noted that a description of the IBM Interpreter and Cardatype (card operated typewriter) were omitted.

Part 2 is devoted to a description of case histories of punched card applications. These include interesting accounts of the use of punched cards (a) in analyzing the subject matter of publications and correspondence pertaining to nickel compounds and nickel catalysts; (b) applied to the results of corrosion tests; (c) based on word coding as well as on the Dyson and National Research Council codes; (d) for indexing reports; (e) for identification of unknown substances through the optical properties of crystals and other physicochemical data; (f) for indexing organic compounds by means of a code based on the Beilstein system; (g) for patent searching as conducted by the Plastics Division of Imperial Chemical Industries; (h) for preparing reports, papers and books (the described technique was used in the preparation of a review on organosilicon compounds published in "Chemical Reviews"); (i) for abstracting and providing information service on plant breeding and genetics; (j) for anesthesia records; (k) for routine library operations; (l) for general use in industry; (m) for production control in a textile finishing plant and in screw manufacture; and (n) for keeping inventory records.

Part 3 is concerned with some of the fundamental problems involved in the use of punched card techniques. A mathematical analysis of coding systems is presented and a description is given of the use of punched cards in the correlation of research data and of a number of the leading chemical codes. The balance of this section of the book is devoted to a discussion of indexing and index searching, literature and patent searching, classification, transcription problems and use of punched cards in scientific computations. There is some doubt in the mind of the reviewer as to the justification of including certain of the chapters in Part 3 in a book entitled "Punched Cards."