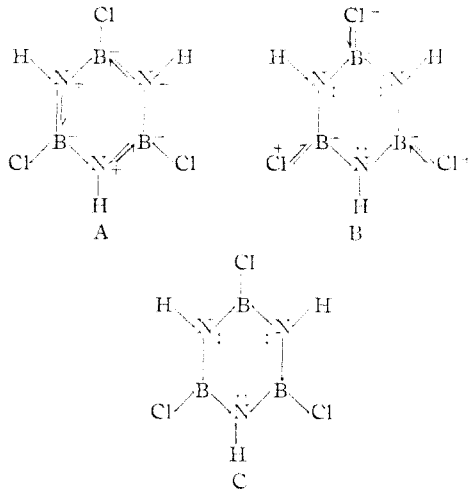

Fig. 1.

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.

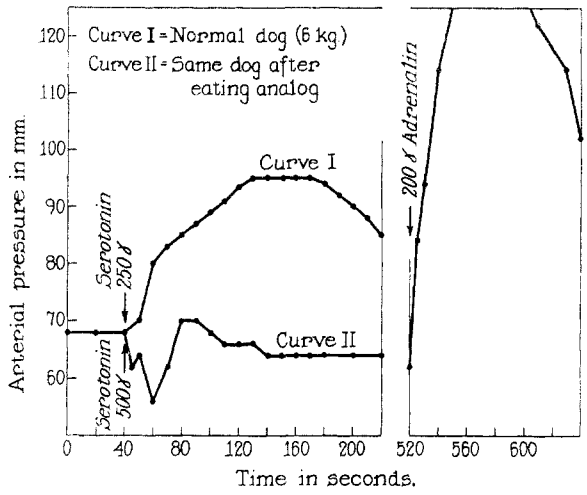

Fig. 1.

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).