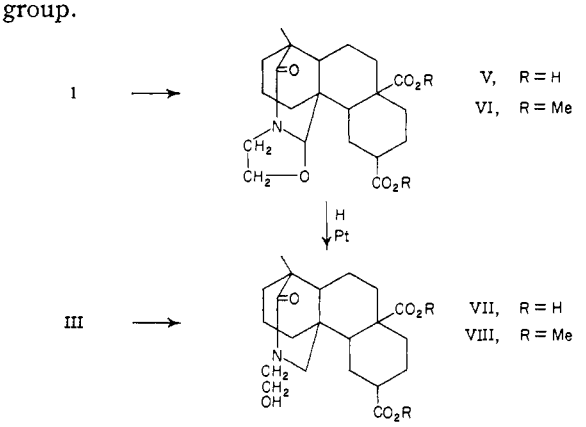
without rupture of the oxide ring, while with isoatisine oxidation proceeds with rupture of the oxide ring, introduction of the lactam carbonyl at the site of rupture and the formation of a free $-NCH_2CH_2OH$ group.



THE ROCKEFELLER INSTITUTE
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RECEIVED JULY 19, 1954

AMEBACIDAL ACTIVITY OF PUROMYCIN[1] IN THE GUINEA PIG

Sir:

In the course of the screening program being conducted in this laboratory for the evaluation of potential amebacidal agents, it has been observed that Puromycin (Lederle), an antibiotic form *Streptomyces albo-niger*, possesses significant activity against experimenally induced *Endamoeba histolytica* infections in the guinea pig. Thisco mpound has previously been reported to have significant activity against trypanosomiasis infections in experimental animals.[2,3] The structure of Puromycin has recently been elucidated.[4]

The test procedure for our amebiasis program has been described by Taylor and Greenberg.[5] All compounds are administered orally in solution, twice daily for five days. Simaroubidin (Merck) is used as the reference drug. At its minimum effective dosage of 2.5 mg./kg. of body weight, more than 98% of the infections are cured by it.

Puromycin (as the dihydrochloride) was initially tested at levels of 50 and 25 mg./kg. of body weight. At these levels the compound was highly effective against the induced amebic infections in the guinea pig. The drug has now been tested at lower levels, and the minimum effective dosage has been established at 6.25 mg. of the dihydrochloride per kg. of body weight, equivalent to 5.40 mg. of the free base. This compares with an oral LD_{50} for the dihydrochloride in non-inoculated guinea pigs of 600 mg./kg. of body weight (19/20 confidence limits), equivalent to 520 mg./kg. of the free base.

At 50 mg./kg., the highest oral dosage level employed to date therapeutically, there has been no evidence of drug toxicity. Several other antibiotics (Terramycin, Aureomycin, Chloromycetin, etc.) similarly tested produced weight loss and severe diarrhea. These toxic manifestations appeared following the fourth dose of the test compound. Diarrhea and weight loss due to amebic infection do not ordinarily appear until seven to nine days after intracecal injection of the parasites.

The amebacidal activity of seven antibiotics has previously been reported from this laboratory[5]; three additional ones have now been tested along with Puromycin. All three of the latter were ineffective at the dosages employed, *viz.*, erythromycin (Erythrocyn, Abbott), up to 50 mg./kg.; Magnamycin (Pfizer), up to 100 mg./kg.; and tetracycline (Tetracyn, Pfizer, Roerig), up to 50 mg./kg.

Analogs and degradation products of Puromycin are now being tested for their amebacidal activity.

NATIONAL MICROBIOLOGICAL INSTITUTE
NATIONAL INSTITUTES OF HEALTH
PUBLIC HEALTH SERVICE
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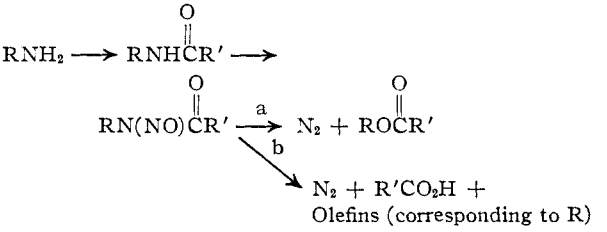
RECEIVED JULY 28, 1954

A NEW METHOD FOR THE DEAMINATION OF ALIPHATIC AMINES

Sir:

I wish to report a new method for the deamination of aliphatic amines. The steps involved are: acylation of the amine, nitrosation of the amide, and thermal elimination of nitrogen from the resulting N-alkyl-N-nitrosoamide.[1]



The two reaction paths account quantitatively for the nitrosoamide used. The esters from path *a* are relatively free of isomers and obtained in high yield, in marked contrast to the products from the classical deamination procedure with nitrous acid.[2]

Standard procedures were used for the acylations and some of the nitrosations. A more convenient method for nitrosating the amide (1 mole) was developed using nitrogen tetroxide[3] (1.5 moles) in the presence of anhydrous sodium acetate (3 moles) at

(1) In earlier publications, this compound was referred to as Achromycin, the name now applied by the Lederle Laboratories to their brand of tetracycline.

(2) J. N. Porter, R. I. Hewitt, C. W. Hesseltine, G. Krupka, J. A. Lowery, W. S. Wallace, N. Bohonos and J. H. Williams, *Antibiotics and Chemotherapy*, **2**, 409 (1952).

(3) R. I. Hewitt, W. S. Wallace, A. R. Gumble, E. R. Gill and J. H. Williams, *Am. J. Trop. Med. Hyg.*, **2**, 254 (1953).

(4) C. W. Waller, P. W. Fryth, B. L. Hutchings and J. H. Williams, THIS JOURNAL, **75**, 2025 (1953).

(5) D. J. Taylor and J. Greenberg, *Am. J. Hyg.*, **56**, 58 (1952).

(1) Previous studies in this field have been concerned largely with the conversion of nitrosoamides into diazoalkanes. M. F. Chancel (*Bull. soc. chim. France*, (3) **13**, 125 (1895)) and H. v. Pechmann (*Ber.*, **31**, 2640 (1898)), however, have noted the instability of the nitrosoamides and the formation of esters from their decomposition; other than these observations, no pertinent work has been reported.

(2) For the reaction of nitrous acid with *n*-butylamine, F. C. Whitmore and D. P. Langlois (THIS JOURNAL, **54**, 3441 (1932)) report *n*-butanol (25%), *sec*-butanol (13%), 1-chlorobutane (5%), 2-chlorobutane (2%), and butenes (37%).

(3) Standard solutions (1–2 *M* in N_2O_4) were prepared by passing NO_2 into carbon tetrachloride or acetic acid at 0°.