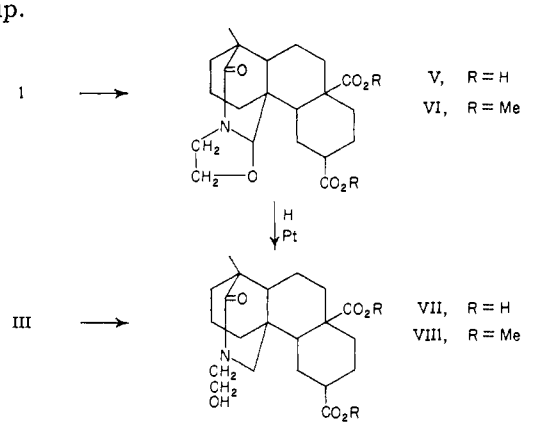
without rupture of the oxide ring, while with isoatisine oxidation proceeds with rupture of the oxide ring, introduction of the lactam carbonyl at the site of rupture and the formation of a free $-NCH_2CH_2OH$ group.



THE ROCKEFELLER INSTITUTE
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NEW YORK 21, NEW YORK
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WALTER A. JACOBS

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
U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
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JOHN F. SHERMAN
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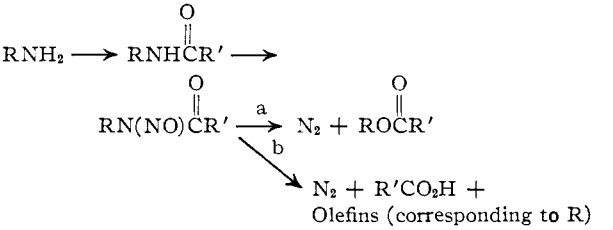
RECEIVED JULY 28, 1954

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).

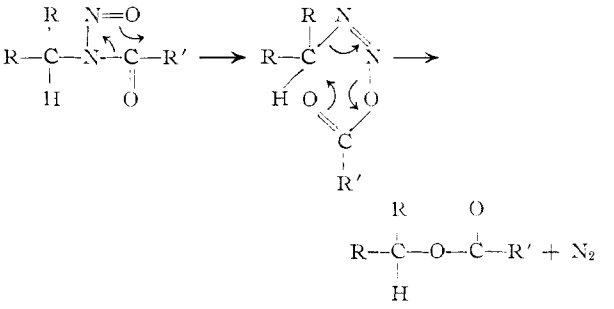
(1) Previous studies in this field have been concerned largely with the conversion of nitrosoamides into diazoalkanes. M. F. Chancel (*Bull. soc. chim. France*, (3) **13**, 125 (1895)) and H. v. Pechmann (*Ber.*, **31**, 2640 (1898)), however, have noted the instability of the nitrosoamides and the formation 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°.

0° (10–20 min. required). A 0.2 *M* solution of N-(*n*-butyl)-N-nitroso-3,5-dinitrobenzamide (m.p. 63–63.5° dec., *Anal.* Calcd. for $C_{11}H_{12}O_6N_4$: C, 44.60; H, 4.08; N, 18.91. Found: C, 44.88; H, 3.95; N, 18.88. I.R.: C=O, 5.81 μ; N=O, 6.52 μ) in hexane[4] was refluxed for 15 hr. to yield nitrogen, 1-butene,[5] 3,5-dinitrobenzoic acid (17–19%), and *n*-butyl DNB (80–82%) (DNB = 3,5-dinitrobenzoate); m.p. (crude product) 62–63°, lit.[6] 64°. The infrared spectrum of the crude ester was superimposable[7] in detail on that of an authentic sample of *n*-butyl DNB. Similarly, the *iso*-butyl analog yielded nitrogen, 2-methylpropene, 3,5-dinitrobenzoic acid (33%), *iso*-butyl DNB (62%), *sec*-butyl DNB (3%), and *tert*-butyl DNB (1%). The analogous nitrosobenzamides and nitrosoacetamides gave identical yields of the respective esters, whereas the nitrososulfonamides and nitrosourethanes gave lower yields (15% less) of the sulfonates and carbonates, respectively. The N-nitroamides were also found to be thermally labile, forming nitrous oxide and esters; the yields of the latter were the same as those from the related nitrosoamides.

Work in progress on optically active *sec*-butyl nitrosoamides has shown that *retention* of configuration occurs in the reaction. The intramolecular nature of the reaction is shown by the elimination of nitrogen from N-(*sec*-butyl)-N-nitrosobenzamide in excess acetic acid to yield some *sec*-butyl acetate, but predominantly *sec*-butyl benzoate. On the basis of the latter facts, the nature and yields of the reaction products, and other evidence to be reported later, the following mechanism is proposed for the reaction.[8] The nitrogen elimination step, therefore, represents a new type of S_Ni reaction.[9]



(4) The yields of reaction products are relatively independent of the solvent used; however, the purest esters and the highest yields were obtained in non-polar solvents.

(5) Infrared spectra indicate pure 1-butene. In one experiment, perbenzoic acid titration gave 16% olefin.

(6) R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," John Wiley and Sons, New York, N. Y., 1948, pp. 226.

(7) A comparison with spectra of standard mixtures of the *n* and *sec* butyl esters, indicates that less than 1% of the *sec* isomer could have been formed in the reaction.

(8) The cyclic six-membered transition state as pictured represents a simplified way to indicate the S_Ni reaction. Our data indicate that the mechanism is actually more complex and not as synchronous as pictured.

(9) W. A. Cowdrey, E. D. Hughes, C. K. Ingold, S. Masterman and A. D. Scott, *J. Chem. Soc.*, 1267 (1937).

STERLING CHEMISTRY LABORATORY
YALE UNIVERSITY EMIL H. WHITE
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RECEIVED JULY 6, 1954

BOOK REVIEWS

Structure and Properties of Solid Surfaces. Edited by ROBERT GOMER and CYRIL STANLEY SMITH. The University of Chicago Press, 5750 Ellis Avenue, Chicago 37, Illinois. 1953. xvi + 491 pp. 14.5 × 22 cm. $8.50.

This book is a carefully edited collection of fourteen papers and of the discussion attending their presentation at a conference sponsored by the National Research Council at Lake Geneva, Wisconsin, in September 1952. In the preface, one of the authors adequately summarizes the purpose of the book and conference as follows: "The great practical importance of surfaces is equaled by their purely scientific interest. Although we have skillfully harnessed surface properties, much of our success is the result of luck and intuition, and many fascinating problems remain unsolved. It was the purpose of the conference which gave rise to this book to throw some light on these problems. In particular, it was hoped to find common denominators for different aspects of surface study by combining contributions from many fields."

The nature of the subject matter of the book and the high quality of presentation can be judged from the following table of contents and authors: I, "The Use of Classical Macroscopic Concepts in Surface-Energy Problems" by Conyers Herring; II, "Atomic Theory of Surface Energy" by P. P. Ewald and H. Juretschke; III, "The Mechanical Properties of Crystalline Metal Surfaces" by A. J. Shaler; IV, "Wetting of Solids as Influenced by the Polarizability of Surface Ions" by W. A. Weyl; V, "The Study of Solid Surfaces" by George P. Thomson; VI, "The Adhesion of Solids" by F. P. Bowden and D. Tabor; VII, "Crystal Growth and Chemical Structure" by A. F. Wells; VIII, "Some Remarks on Facts and Theories of Crystal Growth" by H. E. Buckley; IX, "Epitaxy" by H. Seifert; X, "Physical Adsorption of Gases on Solids" by Terrell L. Hill; XI, "Surface Structure from the Standpoint of Chemisorption and Catalysis" by M. Boudart; XII, "Physical and Chemical Adsorption of Gases on Iron Synthetic Ammonia Catalysts" by P. H. Emmett; XIII, "Chemisorption on Solid Surfaces" by Ahlborn Wheeler; XIV, "The Catalytic Action of Spinels" by G.-M. Schwab, E. Roth, Ch. Grintzos and N. Mavrakis.

In addition to the above mentioned authors, the following individuals, most of whom are recognized authorities in their various fields, participated in the rather extended discussions: J. A. Becker, R. F. Brill, Stephen Brunauer, N. Cabrera, Robert Gomer, A. Guinier, George Jura, J. E. Mayer, Erwin W. Müller, LeRoy G. Schulz, Cyril S. Smith, I. N. Stranski, David Turnbull, Carl Wagner and Adrienne R. Weill.

The coverage of the subject matter is both thorough and critical. The book, like the conference itself, represents a real contribution by virtue of its being a coöperative effort by a number of specialists in a field that is too large to be covered authoritatively by any one individual. Furthermore, the format, the freedom from typographical errors, and the general excellence of editing seem to this reviewer to set a standard that may well be emulated by those organizing and publishing the papers and discussions of other scientific conferences and symposia.