COMMUNICATIONS TO THE EDITOR

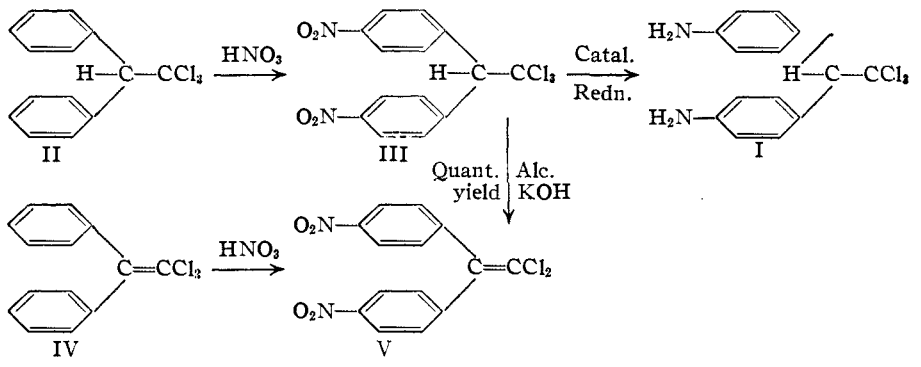
THE ANTITUBERCULAR ACTION OF 1,1,1-TRICHLORO-2,2-BIS-(*p*-AMINOPHENYL)-ETHANE

Sir:

In 1945 work was commenced at the Chemical Warfare Laboratories in Ottawa on the synthesis of the compound 1,1,1-trichloro-2,2-bis-(*p*-aminophenyl)-ethane (I).[1] It appeared from studies carried out on the Läuger hypothesis for the mechanism of action of DDT,[2] using fluorine analogs,[3,4] that this compound might possess marked antitubercular activity.

In view of similar work recently reported by Burger, Graef and Bailey,[5] we wish to report the progress of these researches at this time.

The synthesis of I seemed possible by the route



since the work of Lange and Zufall[6] showed that 1,1-dichloro-2,2-bis-(phenyl)-ethylene (IV) gave the compound 1,1-dichloro-2,2-bis-(*p*-nitrophenyl)-ethylene (V) as the main product of nitration.

The nitration of 1,1,1-trichloro-2,2-bis-(phenyl)-ethane (II) proceeded smoothly and a crystalline dinitro compound melting at 166–167° uncor. was isolated in good yield from the reaction mixture. This product was shown to be 1,1,1-trichloro-2,2-bis-(*p*-nitrophenyl)-ethane (III) by dehydrochlorination to V. The product from the dehydrochlorination proved to be identical with V prepared by the method of Lange and Zufall. Upon catalytic hydrogenation compound III took up six moles of hydrogen. The resulting amine was unstable in the crude form but was much more stable when purified by a procedure which will be described later. The substance crystallizes in the form of platelets melting with decomposition from 92–95° (uncor.) (calcd. for $C_{14}H_{13}N_2Cl_3$: N, 8.88. Found: N, 8.80). Repeated recrystallization of an analytically pure sample failed to raise the melting point or decrease the melting range. This is probably due to decomposition, with loss of hydrogen chloride, near the melting point.

In vitro tests on the activity of I showed that it gave complete inhibition of growth of *Mycobacterium tuberculosis* at dilutions of 1/100,000 and some inhibition at dilutions of 1/1,000,000. Transfer experiments showed that at dilutions of 1/100,000 the compound was bactericidal while at 1/1,000,000 it was bacteristatic. *In vivo* tests on the antitubercular activity of I, using the short assay of Feldman and Hinshaw,[7] showed remarkable control of experimentally induced tuberculosis in guinea pigs. The compound was fed at a level of 0.5% of the ration, this being the maximum well tolerated dose. The blood of guinea pigs fed this level of drug for a period of 56 days was found to contain an average of 1 mgm.% of I as determined by the method of Marshall.[8] This method has proven entirely satisfactory for the determination of I in biological material as well as in pure solution.

Full experimental details will be published later.

(1) Research Reports, Chemical Warfare Laboratories, Department of National Defense (army), Ottawa, Canada.

(2) P. Läuger, H. Martin and P. Müller, *Helv. Chim. Acta*, **27**, 892 (1944).

(3) S. Kirkwood and J. R. Dacey, *Can. J. Research*, **24B**, 69 (1946).

(4) S. Kirkwood and P. H. Phillips, *J. Pharmacol. and Exp. Therap.*, **87**, 375 (1946).

(5) A. Burger, E. Graef and M. S. Bailey, THIS JOURNAL, **68**, 1725 (1946).

(6) K. Lange and A. Zufall, *Ann.*, **271**, 1 (1893).

(7) W. H. Feldman and H. C. Hinshaw, *Am. Rev. Tuberc.*, **51**, 582 (1945).

(8) E. K. Marshall, *Proc. Soc. Exptl. Biol. Med.*, **36**, 422 (1937).

THE DEPARTMENTS OF BIOCHEMISTRY AND AGRICULTURAL BACTERIOLOGY
UNIVERSITY OF WISCONSIN
MADISON 6, WISCONSIN
SAMUEL KIRKWOOD
PAUL H. PHILLIPS
ELIZABETH MCCOY

RECEIVED SEPTEMBER 26, 1946

STREPTOMYCES ANTIBIOTICS. XI. THE STRUCTURE OF TETRAACETYLBISDESOXYSTREPTOBIOSAMINE

Sir:

Treatment of ethyl tetraacetylthiostreptobiosaminide diethyl mercaptal[1] with Raney nickel catalyst gave tetraacetylbisdesoxystreptobiosamine[1] and tetraacetyldesoxystreptobiosamine (m. p. 166–167°, $[\alpha]^{25}D$ −81° (*c*, 1.04 in chloroform). *Anal.* Calcd. for $C_{13}H_{21}NO_8(CH_3CO)_4$:

(1) (a) Kuehl, Flynn, Brink and Folkers, THIS JOURNAL, **68**, 2096 (1946); (b) Hooper, Klemm, Polglase and Wolfrom, *ibid.*, **68**, 2120 (1946).