Fraction	B. p. °C.	Mm.	Grams	$n^{25}D$	$[\alpha]^{25}D$
1	45–46.5	4	1.3	1.4909	+5.1
2	46.5–80	4	2.9	1.4932	+5.1
3	80–89	4.5	0.7	1.5110	...
4	89–95	5	1.9	1.5095	+2.4

Fraction 1 was concluded to be essentially pure α-phenethyl nitrite. In order to establish the nature of fraction 4, 50 g. of *dl*-α-phenethyl chloride was treated with silver nitrite under the conditions described above, and from the crude reaction product there was obtained by repeated fractionation, in addition to 11.5 g. of α-phenethyl nitrite of b. p. 34–36° at 2 mm. and of $n^{25}D$ 1.4938, 2.5 g. of colorless oil of b. p. 90–95° at 3 mm. and of $n^{25}D$ 1.5210. The latter material,.which corresponded roughly to fraction 4 above, was shown to contain largely α-nitroethylbenzene by conversion to the aci-form according to the method of Bamberger and Seligman.[6] The intermediate fractions gave precipitates of silver chloride when warmed with alcoholic silver nitrate solution and were concluded to contain, in addition to the other two components, unreacted α-phenethyl chloride.

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(6) Bamberger and Seligman, *Ber.*, **36**, 707 (1903).

CONVERSE MEMORIAL LABORATORY
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Catalytic Decomposition of DDT

BY A. L. FLENNER

From work conducted on the stability of DDT to heating at 115°, Fleck and Haller[1] concluded that impurities present in technical DDT inhibit the action of catalytic substances in eliminating hydrogen chloride, and that removal of these impurities without simultaneous removal of catalytic substances produces an apparent instability of DDT. In the course of work on the manufacture and formulation of DDT, this Laboratory made a study of the stability of samples varying in degrees of purity.

It was found that Technical DDT, having a set point of 88°, and highly purified material, with a melting point of 108.5°, evolved no hydrogen chloride when heated for twenty-four hours at 115°, whereas material which had been once recrystallized from ethanol, and having a melting point of 105–107°, did evolve hydrogen chloride when heated under the same conditions. The material melting at 105 to 107° had not been filtered from a small amount of insoluble impurities during the recrystallization and it was thought that these impurities might be acting as catalytic decomposing substances. A portion of the partially purified material was therefore dissolved in ethanol, filtered, and then the solution evaporated to dryness to recover the DDT. When this filtered DDT, after drying, was subjected to heating at 115° for twenty-four hours, it was found to be stable since no hydrogen chloride was evolved, which indicates that the insoluble impurities acted as catalytic decomposition agents and their removal rendered the DDT stable under the test conditions. To obtain additional evidence, both technical DDT and purified DDT of m. p. 108.5° were heated in the presence of iron oxide at 115°. Hydrogen chloride was evolved almost immediately from different samples of the purified material, while from four to six hours were required to evolve hydrogen chloride from samples of technical DDT.

These results therefore verify those of Fleck and Haller[1] and it is concluded that there is some substance or substances present in technical DDT which act as an inhibitor to the catalytic elimination of HCl. Removal of these inhibiting substances will render the DDT susceptible to catalytic decomposition. It, therefore, seems quite possible that under conditions of use technical DDT may be more stable than purified or partially purified material since catalytic substances present in diluents and natural dusts may act to liberate hydrogen chloride slowly from spray deposits of the purified DDT. Although purified DDT is not being used extensively at the present time any future use under field conditions may require the addition of an inhibitor to protect it from catalytic decomposition.

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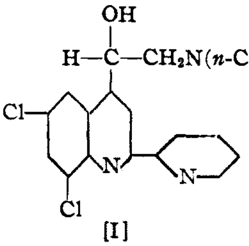
(1) Fleck and Haller, THIS JOURNAL, **68**, 142 (1946).

PEST CONTROL RESEARCH LABORATORY
E. I. DU PONT DE NEMOURS & CO., INC.
WILMINGTON, DELAWARE RECEIVED AUGUST 5, 1946

6,8-Dichloro-2-(2'-pyridyl)-α-di-*n*-butylaminomethyl-4-quinolinemethanol[1a]

BY HENRY GILMAN, LEO TOLMAN AND SAMUEL P. MASSIE, JR.

In connection with studies on experimental avian malaria it was desirable to determine the activity of a 6,8-dichloro-4-quinolinemethanol having a nitrogen heterocycle in the 2-position. The compound selected was 6,8-dichloro-2-(2'-pyridyl)-α-di-*n*-butylaminomethyl-4-quinolinemethanol.[1b] This compound [I] was prepared *via* the Pfitzinger reaction by condensation of 5,7-dichloroisatin with methyl α-pyridyl ketone.[2] Ethyl 6,8-dichloro-2-(2'-pyridyl)-cinchoninate was prepared incidental to an examination of its condensation with ethyl acetate to give the corresponding ketoester. The plan was to brominate the keto-ester as a means of preparing the 4-bromoacetyl compound. However, some orienting experiments showed that the condensation of the ethyl ester with ethyl acetate by means of sodium ethoxide was not so satisfactory as the reaction of diazomethane with the acid chloride.



[I]

Experimental

6,8-Dichloro-2-(2'-pyridyl)-cinchonic Acid.—A mixture of 77 g. (0.36 mole) of 5,7-dichloroisatin,[3] 60 g. (1.08

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(1) (a) The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Iowa State College; (b) the Survey Number assigned to this drug by The Survey of Antimalarial Drugs is SN-14,143-4. The activities of these compounds will be tabulated in a forthcoming monograph.

(2) See Winstein, Jacobs, *et al.*, THIS JOURNAL, **68**, 1831 (1946). Also, Lindwall, Bandes, and Weinberg *ibid.*, **53**, 317 (1931).

(3) Prepared in accordance with directions kindly provided by Drs. H. Sargent and T. C. Myers of the California Institute of Technology.

moles) of potassium hydroxide in 150 cc. of water, and two liters of ethanol was heated to reflux with stirring, and 44 g. (0.36 mole) of methyl α-pyridyl ketone was added rapidly. After working up the reaction product by customary procedures there was obtained 100 g. (87%) of product melting at 328–330°. An analytical sample of this acid was prepared by dissolving a small portion in hot dilute potassium hydroxide solution and heating with Norite. The warm filtrate was neutralized with acetic acid, and the solid obtained in this manner was filtered and washed with hot ethanol. After drying in the oven at 130°, the compound melted at 336–337°.

Anal. Calcd. for $C_{15}H_8O_2N_2Cl_2$: Cl, 22.18; N, 8.78. Found: Cl, 21.99; N, 8.95.

Ethyl 6,8-Dichloro-2-(2′-pyridyl)-cinchoninate.—The acid was esterified by heating 45 g. (0.14 mole) with 250 cc. of absolute ethanol, and 100 cc. of sulfuric acid at the reflux temperature for eight hours. Recrystallization from ethanol (1800 cc.) gave 35 g. (72%) of product melting at 113–114°. The same melting point was observed after recrystallization from ethyl acetate.

Anal. Calcd. for $C_{17}H_{12}O_2N_2Cl_2$: N, 8.05; Cl, 20.43. Found: N, 7.81; Cl, 20.19.

6,8-Dichloro-2-(2′-pyridyl)-cinchoninyl Chloride.—From twenty-five grams (0.078 mole) of 6,8-dichloro-2-(2′-pyridyl)-cinchoninic acid and 100 cc. of thionyl chloride there was obtained 28 g. (100%) of material melting at 255–263°. The melting point varied somewhat on different preparations. Another batch melted at 260–268°. The difference in melting points might be due to varying amounts of hydrogen chloride in the product.

6,8-Dichloro-4-(α-bromoacetyl)-2-(2′-pyridyl)-quinoline.—Twenty-five grams (0.074 mole) of 6,8-dichloro-2-(2′-pyridyl)-cinchoninyl chloride was added slowly to 0.3 mole of diazomethane in 900 cc. of dry methylene chloride[4] solution at 5°. Then, following standard procedures, 30 cc. of 48% hydrobromic acid was added. There was obtained 28 g. (95%) of material melting at 229–231°. Recrystallization of a small amount of this material from acetic acid and a few drops of 48% hydrobromic acid gave a product melting at 265–268°.

Anal. Calcd. for $C_{16}H_9ON_2BrCl_2 \cdot HBr$: N, 5.87; Cl, Br, 48.41. Found: N, 6.22 and 6.20; Cl, Br, 47.24.

A low combined-halogen analysis may be explained by the loss of some hydrogen bromide from the weakly basic product.

α-Bromomethyl-6,8-dichloro-2-(2′-pyridyl)-4-quinoline methanol.—A mixture of 20 g. (0.05 mole) of 6,8-dichloro-4-(α-bromoacetyl)-2-(2′-pyridyl)-quinoline, 11 g. of aluminum *i*-propoxide, and 200 cc. of anhydrous *i*-propanol was heated with a water-bath so that slow distillation occurred.[5] The residue was cooled and 100 cc. of 6 *N* hydrochloric acid was added slowly. The solid was filtered and washed with a little 6 *N* hydrochloric acid and about 200 cc. of water. After drying, the product weighed 16.5 g. (83%) and melted at 245–248°. From another preparation, the yield of carbinol melting over a wider range (245–250°) was 97%.

6,8-Dichloro-2-(2′-pyridyl)-α-di-*n*-butylaminomethyl-4-quinolinemethanol.—Five grams (0.012 mole) of α-bromomethyl-6,8-dichloro-2-(2′-pyridyl)-4-quinolinemethanol, 7.8 g. (0.06 mole) of di-*n*-butylamine and 20 cc. of toluene was heated in an oil-bath at 95–100° for fourteen hours.[5,6] The reaction mixture was poured into anhydrous ether and filtered. The filtrate was first distilled on a steam-bath at reduced pressure, and finally the residue was distilled at 0.5 mm. from a boiling water bath to remove the excess of di-*n*-butylamine. The viscous oil that remained was dissolved in a mixture of two parts anhydrous ether to one part acetone. The monohydrochloride was precipitated from this solution by the addition, with vigorous mechanical stirring, of 10-cc. portions of 0.26 *M* ethereal hydrogen chloride.[7] The first three portions of acid gave a total of 3.3 g. (57%) of material melting at 182–184°.[8] An analytical sample of this product melting at 188–190° was obtained by recrystallization from absolute ethanol–ethyl acetate solution.

Anal. Calcd. for $C_{24}H_{29}ON_3Cl_2 \cdot HCl$: N, 8.70; Cl, 22.05. Found: N, 8.71; Cl, 22.08 and 22.07.

Methyl α-Pyridyl Ketone.—Details are given for this preparation because of a 25% improvement in yield.[9] To 1.2 moles of sodium ethoxide in 1100 cc. of warm benzene, prepared from 27.6 g. (1.2 g. atoms) of sodium sand and 55.2 g. (1.2 mole) of absolute ethanol, was added with vigorous stirring a mixture of 120.2 g. (0.8 mole) of ethyl picolinate[10] and 140.8 g. (1.6 moles) of anhydrous ethyl acetate at a rate to maintain gentle refluxing. During the addition the sodium ethoxide disappeared; the mixture became clear, and then formed a thick yellow mush. The mixture was refluxed with stirring for twelve hours, cooled and poured into a cold solution of 40 g. of sodium hydroxide in 800 cc. of water. The light yellow solid was filtered off and 800 cc. of water was added to the filtrate. The benzene and aqueous layers were separated. The benzene layer was extracted with 400 cc. of water and the combined aqueous layers extracted with 100 cc. of benzene. The yellow precipitate was suspended in the aqueous solution and the mixture acidified with 350 cc. of concentrated hydrochloric acid. The solution was refluxed for two hours, cooled, made basic with solid sodium carbonate and extracted with 1500 cc. of ether in two portions. The ether was dried over anhydrous sodium sulfate. Removal of the ether and distillation of the residue at 79–80° (10 mm.) gave 72 g. (75%) of methyl α-pyridyl ketone.

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(4) The authors are grateful to Dr. Robert E. Lutz for general directions on the use of methylene chloride in this reaction.

(5) This procedure followed a general method of Dr. Robert E. Lutz for the preparation of the corresponding 2-phenyl derivative.

(6) The temperature does not appear to be very critical in this condensation as good yields were obtained by heating at 70°. The period of heating was varied from six to fourteen hours without appreciable change in yield.

(7) It was found helpful in some cases where mixtures of amines were involved to effect separation by fractional precipitation of the hydrochlorides, using dilute ethereal hydrogen chloride.

(8) The melting points vary with the rate of heating. The melting points reported were taken by inserting the tube into the bath at 170° and heating the bath at 8° per minute. The pure compound also melted in twenty-eight seconds when inserted into a constant temperature bath of 198–199°.

(9) Kolloff and Hunter, THIS JOURNAL, **63**, 490 (1941).

(10) This ester was prepared in 73% yield by the esterification of picolinic acid with ethanol using hydrogen chloride.

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RECEIVED SEPTEMBER 3, 1946

Antitubercular Studies. Bis-(*p*-aminophenyl) Derivatives of Ethyl Ether and Trichloroethane

BY EDITH GRAEF[1] AND ALFRED BURGER

On the basis of the observation[2] that the substitution of other "inhalation-anesthetic" groups for the trichloroethyl group in DDT led to compounds approaching, or rivaling, this insecticide in activity, it seemed advisable to substitute similar groups in 1,1,1-trichloro-2,2-bis-(*p*-aminophenyl)-ethane since one of its acyl derivatives had shown considerable antitubercular activity.[3]

As the first example in this series we have prepared α,α′-bis-(*p*-aminophenyl)-ethyl ether by condensation of 1-(*p*-acetamidophenyl)-ethyl bromide with sodium 1-(*p*-acetamidophenyl) eth-

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(1) Du Pont Post-Graduate Fellow.

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

(3) Burger, Graef and Bailey, THIS JOURNAL, **68**, 1725 (1946).