Table I. The X-ray crystallography of the *trans* diacetate has been reported by T. N. White.[5]

Experimental

Cyclohexanediol[6] (471 g.), prepared by the catalytic hydrogenation of hydroquinone, was acetylated with 8.12 equivalents of acetic anhydride by refluxing two hours. The acetylation mixture was allowed to stand at room temperature several days. The volatile material was distilled off at 10 mm. on the steam-bath. The distillate weighed 620 g. The residue crystallized on cooling. The diacetate crystals were filtered at 38°, washed twice with a small amount of alcohol and dried *in vacuo*, m. p. 102.5–103.5°.

The mother liquors were poured into water, extracted with ether, dried with anhydrous potassium carbonate, the ether removed and the residue crystallized from about 300 cc. of alcohol. The first crop weighed 280 g. This material was crystallized from petroleum ether (b. r. 30–60°) (Skellysolve "F"). Two forms of crystals were obtained. The *trans* form crystallized as fragile needles, while the *cis* form came down as massive prisms or as rosets. By vigorously shaking the dried product the *trans* crystals were broken up and the *cis* form was easily picked out. The crude *cis* form thus obtained melted at 35–37°. This was dissolved in petroleum ether, and when cold seeded with a well-formed *cis* crystal. The *cis* form crystallized at once. By carefully watching the course of the crystallization it was easy to observe the formation of the first needles of the *trans* diacetate. At this point the liquid was decanted from the *cis* crystals. One or two more crystallizations from petroleum ether sufficed to remove impurities and to yield a *cis* form with a freezing point of 41.25°. Coops, *et al.*, give 39° as the melting point of this isomer. Typical crystals are shown in Fig. 2. The refractive index of the pure *cis* form (supercooled liquid) was $n^{25}D$ 1.4508 and $n^{22.2}D$ 1.4518. The b. p. at 760 mm. was 251°.

Anal. Calcd. for $C_{10}H_{16}O_4$ (*cis*): mol. wt., 200.23; C, 59.98; H, 8.06. Found: C, 60.25; H, 7.98.

Hydrolysis was accomplished by boiling for four hours with four times the weight of barium hydroxide octahydrate in 25 volumes of water. Carbon dioxide was passed in to precipitate excess barium, and the solution filtered, evaporated to dryness, and extracted with acetone. The acetone was concentrated, filtered and the solution allowed to crystallize. The product melted at 112.4–112.8°.

Coops, *et al.*, give 112° as the melting point of the pure *cis* form.

(5) T. N. White, *Z. Krist.*, **80**, 5–17 (1931).

(6) We are indebted to Dr. Nathan L. Drake, at University of Maryland, for supplying us with a generous amount of cyclohexane-1,4-diol.

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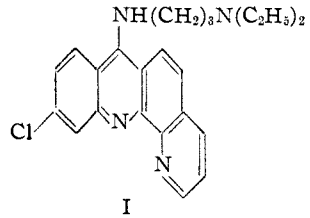
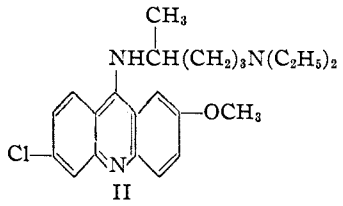
The Preparation of 10-Chloro-7-(3-Diethylaminopropylamino)-pyrid[3,2-*c*]acridine[1]

BY H. R. SNYDER AND HERBERT E. FREIER[2]

During the recent search for new antimalarials it seemed of interest to prepare for testing 10-chloro-7-(3-diethylaminopropylamino)-pyrid[3,2-*c*]acridine (I), which is closely related chemically to atebrin (II) but which has the additional heterocyclic ring.



I



II

By the use of experimental conditions similar to those employed[3] in the condensation of *p*-anisidine with 2,5-dichlorobenzoic acid, 8-aminoquinoline was condensed with 2,4-dichlorobenzoic acid to give 8-(2-carboxy-5-chlorophenylamino)-quinoline in 55% yield. This substance readily underwent the expected cyclization and the product reacted with phosphorus oxychloride to form 7,10-dichloropyrid[3,2-*c*]acridine in 38% yield. The desired drug (I) was obtained by heating the dichloro compound with 3-diethylaminopropylamine at 100–110° for two hours; it was isolated only as the picrate. Because of the fact that it became necessary to abandon the project before the synthesis could be repeated on a preparative scale, the work is being reported in its present form.

Experimental

8-(2-Carboxy-5-chlorophenylamino)-quinoline.—A 150-ml. three-necked flask, fitted with a stirrer and a partial reflux condenser, containing 15 g. of 8-aminoquinoline, 14.3 g. of 2,4-dichlorobenzoic acid, 10.4 g. of potassium carbonate, 0.05 g. of copper bronze and 30 ml. of *n*-hexanol was placed in an oil-bath. The contents were well stirred and the temperature of the oil-bath was kept at 180°. After the solution had been heated for about twenty minutes the contents solidified; however, the mixture was heated for an additional two hours at the above temperature. The pasty brown solid was added to water and the mixture was steam distilled. The brown solution (400 ml.) remaining in the distilling flask was filtered while hot and as the solution cooled the green potassium salt precipitated. After additional water had been added, the mixture was heated to boiling to dissolve the salt. The solution was made acidic with acetic acid and the green solid was collected by filtration and washed with water. The crude product after being dried in an oven at 80° weighed 13 g. (55%).

The substance after recrystallization from xylene melted at 246–249°.

Anal. Calcd. for $C_{16}H_{11}O_2ClN_2$: C, 64.23; H, 3.71. Found: C, 64.45; H, 3.71.

10-Chloro-7-hydroxy-pyrid[3,2-c]acridine.—In a 50-ml. flask was placed a mixture of 7 g. of crude 8-(2-carboxy-5-chlorophenylamino)-quinoline and 12 ml. of

(1) 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 the University of Illinois.

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(3) Feldman and Kopeliowitsch, *Arch. Pharm.*, **273**, 488 (1935).

concentrated sulfuric acid (sp. gr. 1.84). The mixture was heated on a steam-bath for four hours and then poured into 120 ml. of boiling water. After the mixture had been boiled for five minutes, the yellow precipitate was collected by filtration. The moist solid was boiled for five minutes with a solution of 3.5 g. of sodium carbonate in 45 ml. of water, collected by filtration and washed well with water. The crude product weighed 6 g. (92%). After recrystallization from glacial acetic acid the pure yellow compound melted at 315–320° (block).

Anal. Calcd. for $C_{16}H_9OClN_2$: C, 68.46; H, 3.23. Found: C, 68.32; H, 3.21.

7,10-Dichloro-pyrid[3,2-c]acridine.—The experimental conditions were patterned after those of Albert and Ritchie[4] for the preparation of 9-chloroacridine. In a 50-ml. three-necked flask fitted with a stirrer and reflux condenser, 25 ml. of phosphorus oxychloride was heated to 90° and 5 g. of the crude hydroxy compound was added. The temperature of the bath was then raised to 130–140° and maintained at this temperature for two hours. The excess phosphorus oxychloride was removed by distillation and the residual black tarry substance solidified on cooling. This material was added to 20 ml. of ammonium hydroxide and 50 g. of ice and the mixture was stirred vigorously and then filtered. The greenish brown solid melting at 170–200° weighed 4 g. To this material was added 100 ml. of ethyl alcohol; the mixture was heated under reflux for a few minutes and then filtered. A dilute solution of ammonium hydroxide (0.5%) was added to the brown filtrate until precipitation occurred. The mixture was cooled in an ice-bath and the solid was collected on a Büchner funnel. After three recrystallizations, the light green solid melting at 222–225° weighed 2 g. (38%).

Anal. Calcd. for $C_{16}H_8N_2Cl_2$: C, 64.23; H, 2.69. Found: C, 63.99; H, 2.76.

10-Chloro-7-(3-diethylaminopropylamino)-pyrid[3,2-c]acridine.—A mixture of 0.5 g. of the chloro compound and 2 g. of dry 3-diethylaminopropylamine (dried over solid potassium hydroxide for twelve hours and then distilled) was heated at 100–110° for two hours. To the red solution was added 3 ml. of 15% sodium hydroxide and 25 ml. of ether. After the mixture had been stirred the ether layer was separated and washed five times with 10-ml. portions of water to remove any excess 3-diethylaminopropylamine. The ether solution was dried over potassium carbonate, filtered and the solvent was removed by distillation. The residual red oil (0.3 g.) was dissolved in ethyl alcohol and to this solution was added a saturated solution of picric acid in ethyl alcohol. The dipicrate after three recrystallizations from nitromethane melted at 213–216°.

Anal. Calcd. for $C_{35}H_{31}ClN_{10}O_{14}$: C, 49.38; H, 3.67. Found: C, 49.36; H, 3.90.

(4) Albert and Ritchie, "Organic Syntheses," **22**, 5 (1942).

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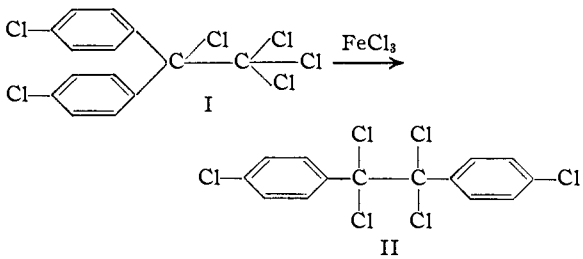
[CONTRIBUTION FROM HERCULES EXPERIMENT STATION, HERCULES POWDER COMPANY]

Rearrangement of 1,1,1,2-Tetrachloro-2,2-bis-(*p*-chlorophenyl)-ethane, "Chloro-DDT," to 1,1,-2,2-Tetrachloro-1,2-bis-(*p*-chlorophenyl)-ethane

BY W. L. WALTON[1]

It has been shown[1a] that 1,1,1-trichloro-2,2-bis-(*p*-chlorophenyl)-ethane (DDT) yields an equivalent of hydrogen chloride and 1,1-dichloro-2,2-bis-(*p*-chlorophenyl)-ethylene when treated with ferric chloride. No rearrangement was involved in this reaction.

In our laboratories a study was made of the effect of anhydrous ferric chloride on the compound in which the tertiary aliphatic hydrogen atom of DDT had been replaced by a chlorine atom. During the course of this work with 1,1,-1,2-tetrachloro-2,2-bis-(*p*-chlorophenyl)-ethane (I) the following interesting rearrangement was observed:



The product "1,1,2,2-tetrachloro-1,2-bis-(*p*-chlorophenyl)-ethane" or, systematically, *p,p'*-$\alpha,\alpha,\alpha',\alpha'$-hexachlorobibenzyl (II) was obtained in 85% yield when molten (I) was heated for fifteen seconds with a trace of ferric chloride. The reaction was strongly exothermic. Long heating of the tetrachloroethane (I) with ferric chloride altered the course of the reaction leading to the evolution of much hydrogen chloride and a dark viscous reaction mixture from which none of (II) could be isolated.

The chief product of this rearrangement, hexachlorobibenzyl (II) is a known compound.[2] In our work its identity was established by synthesis from α,α,α,p-tetrachlorotoluene[2] and by its conversion to the known derivatives 4,4'-dichlorotolane,[2] and 4,4'-dichlorobenzil.[3]

Experimental

Rearrangement.—Fifteen grams of 1,1,1-trichloro-2-chloro-2,2-bis-(*p*-chlorophenyl)-ethane (I)[4] was heated to 160° and 5 mg. of anhydrous ferric chloride was stirred into the melt. The melt turned blue, evolved hydrogen chloride, and its temperature rose rapidly to 210°. The mixture was immediately cooled to room temperature by rapidly transferring the reaction vessel to an ice-water-bath. Solidification began before the temperature indicated by the thermometer reached 170°. The crystalline mass was pulverized under 20 ml. of carbon tetrachloride while being heated on a steam-bath, and then cooled and filtered. The yield of gray-white crude product was 12.75 g. (85% of theoretical); it melted at 189–192°. One recrystallization from carbon tetrachloride raised the melting point to 193–194°. Kenner and Witham[2] reported m. p. 190° (apparently uncorrected).

Anal. Calcd. for $C_{14}H_8Cl_6$: Cl, 54.70. Found: Cl, 55.0.

p,p'-**Dichlorobenzil.**—A mixture of 1 g. of the hexachlorobibenzyl (II), 40 ml. of glacial acetic acid and 10 ml. of water was placed in a sealed Pyrex tube and heated in an oil-bath at 160–175° for thirty-six hours. After cooling to room temperature, the tube was opened and the solid

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(1a) Fleck and Haller, THIS JOURNAL, **66**, 2095 (1944).

(2) Kenner and Witham, *J. Chem. Soc.*, **97**, 1960 (1910).

(3) Liebeman and Homeyer, *Ber.*, **12**, 1971 (1879).

(4) Grummitt, Buck and Jenkins, THIS JOURNAL, **67**, 155 (1945).