

norite, made strongly acid (hydrochloric acid) and chilled. The pasty white solid which separated was filtered. (From the filtrate by addition of alkali, extraction with ether and distillation, 14 g. of the original diaminopentane was recovered, b. p. 59° (6 mm.).) The solid was taken up in water, precipitated as the free base with alkali, filtered and dried. The resulting slightly gummy material was dissolved in benzene and again precipitated as the dihydrochloride by passing in dry hydrogen chloride. The product was recrystallized once from methyl alcohol-ether and once from methyl alcohol-acetone to yield 3.5 g. (27% of the theoretical) of a fine white powder melting at 235–236° with evolution of gas. (An additional 2.0 g. of impure product was obtained by concentration of the alcohol-acetone filtrate. However, repeated attempts to purify this gave a product melting from 220–230° with evolution of gas.)

Anal. Calcd. for $C_{24}H_{31}ClN_4O \cdot 2HCl$: N, 11.21. Found: N, 11.28.

6-Aminoveratronictrile (II).—Fifty-six grams (0.27 mole) of 6-nitroveratronictrile was added slowly and with stirring to a solution of 204 g. (0.90 mole) of stannous chloride dihydrate in 100 cc. of concentrated hydrochloric acid and 350 cc. of glacial acetic acid, using an ice-bath to keep the temperature below 40°. After addition was complete, the mixture was stirred for one hour and allowed to stand (room temperature) for nine hours. The mixture was poured into a mush of excess sodium hydroxide and crushed ice, filtered and washed with water. The solid was dissolved in acetone and filtered. This solution was heated to boiling, and precipitation was initiated by addition of water. After thorough chilling, the product was filtered, washed with a mixture of equal volumes of acetone and water, and dried *in vacuo*. The material so obtained weighed 36.5 g.¹⁰ (76% of the theoretical) and melted at 92–93.5°.

Anal. Calcd. for $C_9H_{10}N_2O_2$: N, 15.72. Found: N, 15.67.

6-*p*-Chlorobenzamidoveratronictrile (IV).—To a solution of 15 g. (0.084 mole) of 6-aminoveratronictrile (II) in 100 cc. of acetone was added 200 cc. of water containing 6.8 g. of sodium hydroxide, followed quickly (to prevent precipitation of the amine from its supersaturated solution) by 14.5 g. (0.082 mole) of *p*-chlorobenzoyl chloride. The solution was stirred vigorously until precipitation appeared to be complete and the odor of the acid chloride was no longer distinguishable. The product was filtered and washed with water. Since this compound is only sparingly soluble, it was refluxed under 100 cc. of acetone, chilled, filtered, and washed with methanol. Twelve grams¹¹ (46%) of a white, finely crystalline material was obtained which melted at 216–217°.

(10) An additional 3.5 g. of the amine was isolated from the filtrate as the *p*-chlorobenzoyl derivative by the Schotten-Baumann procedure, thus giving an accountable yield of reduction product of 83%.

(11) Additional material was obtained by treating the acetone-water filtrate from the reaction with alkali and *p*-chlorobenzoyl chloride.

Anal. Calcd. for $C_{16}H_{13}ClN_2O_3$: N, 8.85. Found: N, 8.90.

2-(*p*-Chlorophenyl)-6,7-dimethoxy-4-hydroxyquinazoline (VI).—Six grams (0.019 mole) of 6-*p*-chlorobenzamidoveratronictrile (IV) was mixed with 50 cc. of water and 15 cc. of dioxane and 20 g. of sodium hydroxide was added; to this warm mixture 50 cc. of 30% hydrogen peroxide was added. After the vigorous reaction had subsided, the mixture was refluxed for fifteen minutes, 25 cc. of peroxide was added and refluxing was continued for one hour. This solution was diluted (water) to 800 cc., acidified (acetic acid), and finally made alkaline (ammonium hydroxide), chilled, filtered and the solid washed with water. The precipitate was suspended in boiling acetone, filtered and washed with acetone (from the acetone filtrate was recovered 0.5 g. of unreacted IV). The white powder weighed 4.5 g. (yield, 82%; conversion, 75%) and melted at 313–314° without decomposition.

Anal. Calcd. for $C_{16}H_{13}ClN_2O_3$: N, 8.85. Found: N, 8.90.

2-(*p*-Chlorophenyl)-4-(1-diethylamino-4-pentylamino)-6,7-dimethoxyquinazoline Dihydrochloride (VIII).—Eleven grams (0.034 mole) of the hydroxyquinazoline (VI) was treated as in the above case of the 7-methoxy analog with 7.5 g. (0.036 mole) of phosphorus pentachloride and 20 cc. of phosphorus oxychloride. After removal of the solvent, 35 cc. of dry pyridine and 7.9 g. (0.050 mole) of 1-diethylamino-4-aminopentane was added and the mixture refluxed for eight hours. The solution was acidified (hydrochloric acid) and steam distilled to remove xylene. A small amount (1.5 g.) of acid insoluble material was filtered, and the free base was precipitated from the filtrate by ammonia. After drying, this somewhat gummy solid was dissolved in methyl alcohol, converted into its dihydrochloride (anhydrous hydrogen chloride), and caused to crystallize by addition of an equal volume of acetone. The product was finally recrystallized twice, once from hot dilute hydrochloric acid¹² and once from alcohol-acetone. The white finely crystalline material weighed 5.5 g. (30% of the theoretical) and melted at 227–229° (dec.).

Anal. Calcd. for $C_{25}H_{35}ClN_3O_2 \cdot 2HCl$: N, 10.57. Found: N, 10.58.

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Summary

Two basically substituted derivatives of the quinazoline series, together with five new intermediates, have been synthesized.

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(12) The addition of a few drops of methyl alcohol helps prevent the tendency to form a gel in aqueous media.