m. p. 187° with decomposition (capillary inserted at 110°). Two recrystallizations from hot water gave colorless crystals which were dried in a desiccator over Drierite; m. p. 189° with decomposition (capillary inserted at 110°).

Anal. Calcd. for $C_{12}H_{10}N_4O_3 \cdot 2H_2O$: C, 48.98; H, 4.80; N, 19.04. Found: C, 49.01; H, 5.00; N, 19.39.

On drying at 75–85° the dihydrate loses two molecules of water. The dihydrate is soluble in acetone, ethanol or hot water.

DL-α-Benzamido-1,2,3-triazole-4-propionic Acid.—In a micro-hydrogenator, 200 mg. of platinum oxide in 7 ml. of glacial acetic acid was pre-reduced. Then, 0.553 g. (0.00188 mole) of crude α-benzamido-1,2,3-triazole-4-acrylic acid dihydrate and 5 ml. of glacial acetic acid were added, and the solution was stirred under hydrogen at atmospheric pressure. During the hydrogenation an addition of 100 mg. of platinum oxide was made to maintain the rate. When the theoretical amount of hydrogen had been absorbed, the reaction was stopped and the catalyst removed. Concentration of the filtrate under reduced pressure gave an oil which crystallized on adding water. The gray product which was removed by filtration and dried at 65° weighed 0.390 g. (79%); m. p. 206–208° with decomposition.

The crude product (0.39 g.) was recrystallized from 18 ml. of hot water, yielding 0.30 g. (61%) of colorless crystals; m. p. 217.5–218.5° with decomposition. An analytical sample was prepared by a second recrystallization from hot water; m. p. 219–220° with decomposition.

Anal. Calcd. for $C_{12}H_{12}N_4O_3$: C, 55.38; H, 4.65; N, 21.53. Found: C, 55.12; H, 4.88; N, 21.24.

This compound is soluble in absolute ethanol and insoluble in ether or acetone.

DL-α-Amino-1,2,3-triazole-4-propionic Acid (III). A. Hydrolysis of the Benzoyl Compound.—Hydrolysis of 0.78 g. (0.0030 mole) of α-benzamido-1,2,3-triazole-4-propionic acid was accomplished by reflux for six hours with 20 ml. of 2.5 *N* hydrochloric acid. After ether extraction and charcoal treatment, the aqueous solution was concentrated under reduced pressure to a colorless oil which was twice dissolved in water and reconcentrated to dryness (wt. 0.56 g., 97%). Aniline was added to a warm solution of the oil in 10 ml. of absolute ethanol until the *p*H was 4–5. After twelve hours at room temperature, the crystalline amino acid was collected, washed with absolute ethanol and ether, giving 0.29 g. (62%) of product decomposing with gas evolution at 260°.

The crude product on recrystallization from water–ethanol gave 0.24 g. (51%) of tiny, colorless crystals decomposing at 266°. A second recrystallization failed to alter the decomposition point.

Anal. Calcd. for $C_5H_8N_4O_2$: C, 38.46; H, 5.16; N, 35.88. Found: C, 38.36; H, 5.38; N, 35.71.

This compound is moderately soluble in cold water and soluble in hot; it is insoluble in absolute ethanol or ether.

B. Hydrogenation of VII.—After pre-treatment of 0.460 g. (0.0027 mole) of recrystallized oximino acid (VII) in absolute ethanol with Raney nickel catalyst, 0.0028 mole of ethanolic hydrogen chloride was added and the solution was stirred with 200 mg. of platinum oxide in a micro-hydrogenator under hydrogen at atmospheric pressure. After seven days the theoretical amount of hydrogen had been absorbed. The solution, from which the catalyst had been removed, was concentrated to dryness under reduced pressure, dissolved in water, filtered, and again concentrated to a brittle, tan solid weighing 0.55 g. After recrystallization from ethanol–ethyl acetate and water–acetone, the crystalline hydrochloride amounted to 0.14 g. and decomposed at 219°.

Without further purification, 0.040 g. of the hydrochloride was treated with the calculated amount of dilute ammonium hydroxide and the solution concentrated to dryness under reduced pressure. Solution of the residue in hot water and the addition of two volumes of ethanol produced colorless crystals. After washing with aqueous ethanol (1:1) and drying at 65°, the amino acid decomposed at 266° and weighed 0.020 g. (17% from VII).

Summary

1,2,3-Triazole-4-ethylamine and DL-α-amino-1,2,3-triazole-4-propionic acid, the triazole analogs of histamine and histidine, as well as N-isopropyl-1,2,3-triazole-4-ethylamine and N-isopropylhistamine have been synthesized for pharmacological study.

CAMBRIDGE 39, MASS. RECEIVED NOVEMBER 4, 1948

[CONTRIBUTION FROM DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

Quinazolines. VIII. The Synthesis of an Amino Alcohol Derived from 2,4-Quinazolinedione-5-carboxylic Acid[1]

BY C. H. WANG AND BERT E. CHRISTENSEN

Methods for the synthesis of 2,4-dimethylquinazoline derivatives with an acetyl-substituent in the 7- and 8-positions have recently been described.[2,3] The 5-isomer, however, could not be synthesized by these procedures due to the difficulties encountered in the attempted preparation of the necessary intermediate 3-acetamino-1,2-diacetylbenzene or 3-acetamino-2-acetylbenzoic acid required for the cyclization.[4]

Since it would be useful to this Laboratory to have a quinazoline compound with an amino alcohol substituent in the 5-position, the possibility of utilizing the easily prepared 2,4-quinazolinedione-5-carboxylic acid (I) as the starting material (see Fig. 1) was studied. This intermediate was converted to the acyl chloride (II), which upon treatment with diazomethane formed the diazoketone and at the same time was simultaneously methylated in the 1,3-positions to yield 5-diazoacetyl-1,3-dimethyl-2,4-quinazolinedione (III). This diazoketone upon treatment with dry hydrogen bromide gas was converted to the bromomethyl ketone (IV); however, one of the methyl substituents (either 1 or 3) was lost in the process.

The bromoacetyl derivative (IV) readily combined with morpholine to yield an aminoketone

(1) The work in this paper was made possible by a grant-in-aid from the Research Corporation. Published with the approval of the Monograph Publications Committee, Oregon State College, as Research Paper No. 134, School of Science, Department of Chemistry.

(2) Christensen, Graham and Griffith, THIS JOURNAL, **67**, 2001 (1945).

(3) Isensee and Christensen, *ibid.*, **70**, 4061 (1948).

(4) Wang, Isensee, Griffith and Christensen, *ibid.*, **69**, 1909 (1947).

(V) which was in turn catalytically reduced to the desired amino alcohol (VI).

In order to confirm the simultaneous methylation of the 1,3-positions of (II) during the diazomethane reaction, the starting material (I) was methylated with excess diazomethane. This gave an ester (methyl 1,3-dimethyl-2,4-quinazolinedione-5-carboxylate (VII)), which was identical with that reported both by Scott and Cohen[5] as well as by Lange, Chisholm and Szabo.[6] These investigators had employed dimethyl sulfate as the methylating agent. The ester (VII) was hydrolyzed to the acid (VIII) which upon chlorination with thionyl chloride gave a good yield of 1,3-dimethyl-2,4-quinazolinedione-5-carbonyl chloride (IX). When the acyl chloride (IX) was treated with diazomethane, a diazoketone identical with (III) was produced. These data confirm the earlier observations of the methylation of the 1,3-positions of 2,4-quinazolinedione-5-carbonyl chloride with diazomethane.

Although VII on the basis of mixed melting point tests was identical with the ester prepared by Scott and Cohen, the acid (VIII) obtained by the hydrolysis of VII, was not the same as the 1,3-dimethyl-2,4-quinazolinedione-5-carboxylic acid reported by these workers.[5,6] Scott and Cohen originally prepared the acid by the direct methylation of I using a limited amount of dimethyl sulfate. In order to confirm the earlier work, the methyl ester (VII) prepared in this Laboratory by the method of Scott and Cohen was hydrolyzed to the free acid. This acid was found to be identical with VIII which was obtained as the hydrolysis product of the ester (VII) (prepared by the diazomethane reaction) and different from the dimethyl acid originally reported by these workers. In order to clarify these results the free acid (X) was again prepared in this Laboratory by the direct methylation procedure of Scott and Cohen; the methylation product was found to be a high melting compound as described by these workers. However, carbon and hydrogen data indicate an incomplete methylation yielding the 1(or 3)-methyl-2,4-quinazolinedione-5-carboxylic acid in place of the 1,3-homolog. Since the earlier deduction had been based on nitrogen analysis only, it is possible that the acid in question was the 1(or 3)-methyl-2,4-quinazolinedione-5-carboxylic acid (X) and not the 1,3-dimethyl homolog as originally reported.

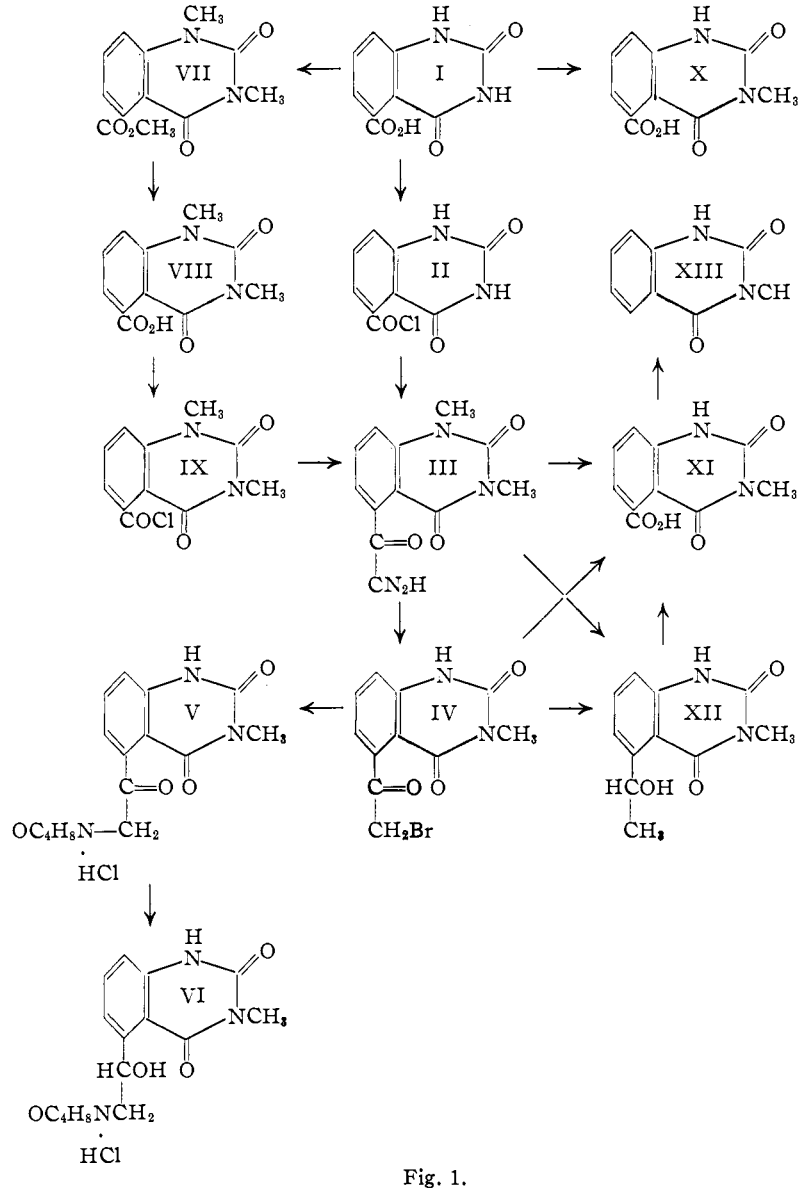

Fig. 1.

Because of the unpredictable ease with which the methyl substituent had been removed during the mild acid treatment of the diazoketone (III), further experiments with III were undertaken. The compound (III) upon oxidation with neutral permanganate again lost a methyl substituent to yield 1(or 3)-methyl-2,4-quinazolinedione-5-carboxylic acid (XI). The loss of a methyl substituent was again observed during reduction

(5) Scott and Cohen, *J. Chem. Soc.*, **119**, 664 (1921).

(6) Lange, Chisholm and Szabo, THIS JOURNAL, **61**, 2170 (1939).

which yields 5-(1-hydroxyethyl-1(or 3)-methyl)-2,4-quinazolinedione (XII). Both the bromomethyl ketone (IV) and the reduction product (XII) after a permanganate oxidation gave acids which on the basis of mixed melting point tests were judged to be identical with XI. From these results, as well as from the analytical data, it was concluded that the same methyl substituent was quantitatively removed during each of the described operations.

The problem of determining the position of the remaining methyl group was approached through decarboxylation experiments. The acid (XI) after removal of the carboxyl group, gave a methyl-2,4-quinazolinedione (XIII) which melted sharply at 198°. This melting point did not agree with 234[7]–237[8]–242°[9] (XIV) reported for the 3-methyl-2,4-quinazolinedione or 147°[8] (XV) or 265°[10] (XVIII) which had been reported for the 1-isomer.

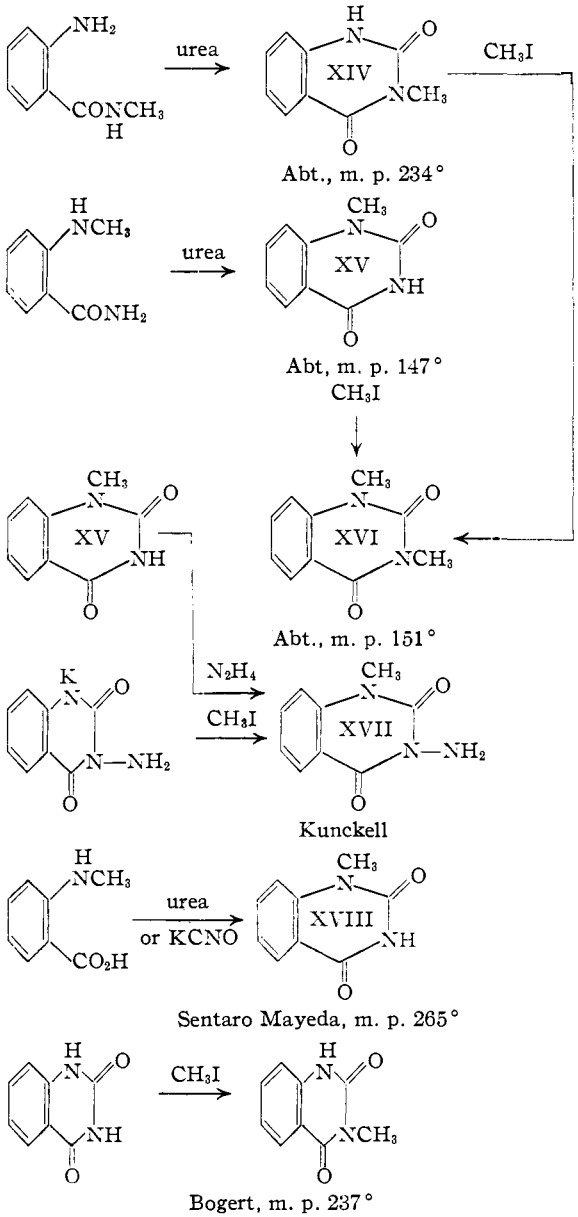

Fig. 2.

A review of the literature reveals that Abt had prepared both the 3- and 1-methyl-2,4-quinazolinediones (XIV) (XV) (m.p.'s 234, 147°) by the cyclization of 2-aminomethylbenzamide and 2-methylaminobenzamide, respectively, with urea (see Fig. 2). Both the 1- and 3-methyl-2,4-quinazolinediones prepared by Abt, after further methylation with methyl iodide, gave an identical known product 1,3-dimethyl-2,4-quinazolinedione (XVI), m.p. 151°.[8] Furthermore, Abt prepared by direct methylation using alkaline methyl iodide, a compound m.p. 147° which he concluded was 1-methyl-2,4-quinazolinedione[8] (XV).

The proof of structure of the 1-methyl isomer m.p. 147° was later confirmed indirectly by the experiments of Kunckell[11] who isolated 3-amino-1-methyl-2,4-quinazolinedione (XVII) as the product of the reaction of the 1-methyl isomer (XV) with hydrazine. The identical compound had previously been obtained by the methylation of the potassium salt of 3-amino-2,4-quinazolinedione, with methyl iodide[11] (see Fig. 2).

On the other hand, Sentaro Mayeda cyclized 2-methylaminobenzoic acid with both urea and potassium cyanate and obtained the same product 1-methyl-2,4-quinazolinedione (XVIII) m.p. 265–266° (see Fig. 2).[10] Confirmation of the existence of (XVIII) m.p. 265–266° was later reported by Seide[12] who prepared this compound by an entirely different series of reactions. Furthermore the experiments of Sentaro Mayeda pertaining to the 1-isomer were confirmed in this Laboratory.

Bogert[7] later reported that the product of the direct methylation of 2,4-quinazolinedione with alkaline methyl iodide was the 3-methyl isomer which he concluded was identical with the 3-methyl-2,4-quinazolinedione (XIV) m.p. 234°, prepared by the cyclization procedures of Abt. Bogert's work has likewise been confirmed in this Laboratory. It is possible that the different results obtained by Bogert and Abt (products m.p. 234° and 147°, respectively) upon direct methylation of 2,4-quinazolinedione may be due to different thermal conditions of the experiments.

In view of the anomalous melting point data, mixed melting point tests were run between each of the following: (1) 3-methyl-2,4-quinazolinedione (XIV), m.p. 242°, prepared by the method of Bogert with a small amount of 1-methyl-2,4-quinazolinedione (XVIII), m.p. 265° prepared by the method of Sentaro Mayeda (also *vice*

(7) Bogert and Scatchard, THIS JOURNAL, **41**, 2062 (1919).
(8) Abt, *J. prakt. Chem.*, [2] **39**, 148 (1889).
(9) Lange and Sheibley, THIS JOURNAL, **55**, 1188 (1933).
(10) Sentaro Mayeda, *C. A.*, **11**, 578 (1916).
(11) Kunckell, *Ber.*, **43**, 1234 (1910).
(12) Seide, *Ann.*, **440**, 331 (1924).

versa); (2) compound (XIV) with the decarboxylation product (XIII), m.p. 198°; (3) compounds (XVIII) and (XIII). In each test there was an appreciable lowering of the melting point which proves that XIII could hardly be a mixture of XIV and XVIII.

One must conclude that there is reasonable support for the structures proposed by Abt and Sentaro Mayeda for both the 1- and 3-methyl-2,4-quinazolinediones. The only data which appear questionable are the melting points, which can best be explained on the basis of, (1) multiple melting points; (2) possibility of isomeric mixtures of 1- and 3-methyl-; or (3) the possibility of stereoisomerism. However, the mixed melting point behavior precludes the first two possibilities, leaving only the alternate explanation, namely, the existence of two stereoisomers of both 1- and 3-methyl-2,4-quinazolinediones. A similar type of isomerism has been reported in the alkaloid literature.[13] If such is the case, then the decarboxylation product (XIII) m.p. 198° appears to be the other stereoisomer of 3-methyl-2,4-quinazolinedione, m.p. 242°.

If XIII is not a stereoisomer of 1(or 3)-methyl-2,4-quinazolinedione then the methyl substituent must be in some other position or attached in some other manner. This would change many of the accepted ideas regarding the methylation products of the quinazolones. For this reason, further detailed studies of this interesting phenomenon are being undertaken by this Laboratory.

Experimental[14]

5-Diazoacetyl-1,3-dimethyl-2,4-quinazolinedione (III).—2,4-Quinazolinedione-5-carboxylic acid (I) was prepared and converted to the corresponding acid chloride by the method of Lange and co-workers. The addition of a few drops of quinoline to the thionyl chloride, besides materially shortening the time of chlorination, gave a purer product.

Twelve and four-tenths grams (0.0553 mole) of 2,4-quinazolinedione-5-carbonyl chloride (II) was pulverized into a fine powder and added gradually with stirring to 600 ml. of an ice-cold benzene solution of diazomethane prepared from 60 g. of N-nitroso-methylurea (0.40 mole of diazomethane). The reaction took place rather slowly as indicated by the rate of evolution of nitrogen gas. After stirring for six hours, the solution was allowed to warm to room temperature and then left standing overnight. The insoluble residue (0.5 g.) was removed by filtration and the solvent concentrated under reduced pressure to 100 ml. After standing in a refrigerator for two days the crystalline diazoketone was removed. The mother liquor was then evaporated to dryness under reduced pressure and the gummy residue redissolved in warm acetone. An additional amount of the diazoketone was obtained by the addition of ether to the acetone solution. The combined fractions weighed 10.1 g. (80%).

For analysis, a portion of the crude diazoketone was recrystallized twice from acetone yielding hard, colorless cubes which on standing decompose, m. p. 157–159°.

Anal. Calcd. for $C_{12}H_{10}O_3N_4$: C, 55.80; H, 3.91; N, 21.70. Found: C, 55.7; H, 3.88; N, 21.7.

The diazoketone was also prepared from 1,3-dimethyl-2,4-quinazolinedione-5-carboxylic acid (VIII) *via* the acyl chloride in a similar manner. The yield in this instance was only 40%.

5-Bromoacetyl-1(or 3)-methyl-2,4-quinazolinedione (IV).—Six grams (0.023 mole) of 5-diazoacetyl-1,3-dimethyl-2,4-quinazolinedione (III) was dissolved in 60 ml. of dry chloroform. The solution was cooled with an ice-bath and then treated with a stream of dry hydrogen bromide until the evolution of nitrogen ceased. The precipitated bromomethyl ketone was filtered, washed with ether and dried in a vacuum. Some additional product was obtained by concentration of the mother liquor. The combined yield weighed 6.6 g. (91%). A portion of this product was recrystallized twice from an alcohol–ether mixture to yield white crystals, m. p. 200–201°.

Anal. Calcd. for $C_{11}H_9O_3N_2Br$: C, 44.44; H, 3.05; N, 9.43; Br, 26.9. Found: C, 44.8; H, 3.15; N, 9.49; Br, 27.3.

5-(2-Morpholine-1-oxoethyl)-1(or 3)-methyl-2,4-quinazolinedione Hydrochloride (V).—Four and five-tenths grams (0.015 mole) of 5-bromoacetyl-1(or 3)-methyl-2,4-quinazolinedione (IV) was suspended in 50 ml. of acetone. To this was added dropwise with shaking 2.6 g. (0.030 mole) of redistilled morpholine. The bromomethyl ketone dissolved gradually accompanied by the precipitation of crystalline morpholine hydrobromide. After standing overnight, the morpholine hydrobromide was removed by filtration and the solvent concentrated under reduced pressure to 10 ml. Fifty milliliters of water was added to the concentrate; the precipitated crude amino ketone was filtered, washed thoroughly with water and vacuum dried. The crude product (m. p. 180° dec.) was then dissolved in 20 ml. of absolute ethanol, cooled with an ice-bath and dry hydrogen chloride gas was bubbled into the solution. The hydrochloride of the amino ketone precipitated upon the addition of dry ether in the form of a voluminous precipitate, which was separated from the mother liquor by means of centrifugation. The product (2 g.) after washing twice with dry ether was a hygroscopic white solid decomposing at about 150°.

Anal. Calcd. for $C_{15}H_{18}O_4N_3Cl$: N, 12.38; ionizable Cl, 10.44. Found: N, 12.5; ionizable Cl, 10.20.

The monopicrate of the amino ketone was prepared by dissolving a sample of the hydrochloride in water and adding saturated aqueous sodium picrate solution. The precipitate obtained after recrystallization from ethanol–ether mixture was a yellow mass. On heating, it turned brownish in color at about 120° and decomposed at 140°.

Anal. Calcd. for $C_{21}H_{20}O_{11}N_6$: C, 47.35; H, 3.80; N, 15.78. Found: C, 47.7; H, 4.03; N, 15.6.

5-(2-Morpholine-1-hydroxyethyl)-1(or 3)-methyl-2,4-quinazolinedione Hydrochloride (VI).—A solution containing 0.56 g. (0.0016 mole) of the amino ketone hydrochloride (V) and 50 ml. of dry methanol was reduced in a low-pressure hydrogenation apparatus at 30 p. s. i. pressure in the presence of 200 mg. of 10% palladium-on-carbon catalyst. After shaking for two hours, the catalyst was removed by filtration and the solution concentrated to 10 ml. The amino alcohol hydrochloride precipitated by the addition of dry ether was separated by centrifuging and yielded 0.30 g. (53%) of a slightly colored, very hygroscopic solid. For analysis, a portion of this product was reprecipitated twice from ethanol with dry ether, yielding a very hygroscopic white mass which decomposed without melting at about 200°.

Anal. Calcd. for $C_{15}H_{20}O_4N_3Cl$: N, 12.30; ionizable Cl, 10.38. Found: N, 12.52; Cl, 10.50.

The monopicrate was prepared by adding a saturated aqueous sodium picrate solution to an aqueous solution of the amino alcohol hydrochloride. The product after recrystallization from an alcohol–ether mixture was a yellow solid decomposing at about 150°.

Anal. Calcd. for $C_{21}H_{22}O_{11}N_6$: C, 47.17; H, 4.16; N, 15.72. Found: C, 47.6; H, 4.16; N, 15.6.

1,3-Dimethyl-2,4-quinazolinedione-5-carboxylic Acid (VIII).—Five grams (0.023 mole) of 2,4-quinazolinedione-

(13) Willstätter, *Ber.*, **29**, 936 (1896); Willstätter and Muller, *ibid.*, **31**, 1202 (1898); Hess, *ibid.*, **52**, 1622 (1919).

(14) All melting points are corrected.

5-carboxylic acid (I) was added in portions with stirring to 200 ml. of an ice-cold ethereal solution of diazomethane prepared from 20 g. of N-nitrosomethylurea (0.13 mole of diazomethane). The reaction appeared to take place rapidly as evidenced by the vigorous evolution of nitrogen gas. After standing at room temperature for six hours, the filtered ethereal solution was evaporated to dryness to yield 4.0 g. (66%) of slightly colored crystals. The crystals were purified by two recrystallizations from ethanol yielding 3.1 g. of colorless product, m. p. 142–143°. This product (VII) was found to be identical with the ester obtained by Lange, Chisholm and Szabo from the complete methylation of 2,4-quinazolinedione-5-carboxylic acid with dimethyl sulfate and sodium hydroxide.

Three grams (0.012 mole) of the ester was hydrolyzed by refluxing with 20 ml. of 20% hydrochloric acid for three hours; toward the end of the hydrolysis, colorless crystals separated out. After standing in the refrigerator overnight, the mixture was separated by filtration giving 2.0 g. (70%) of needles. A portion of this product was recrystallized from ethanol for analysis, m. p. 250–253°.

Anal. Calcd. for $C_{11}H_{10}O_4N_2$: C, 56.39; H, 4.31; neut. equiv., 234. Found: C, 56.8; H, 4.50; neut. equiv., 238.

1,3-Dimethyl-2,4-quinazolinedione-5-carbonyl Chloride (IX).—One and six-tenths grams (0.072 mole) of 1,3-dimethyl-2,4-quinazolinedione-5-carboxylic acid (VIII) was refluxed for half an hour with 20 ml. of thionyl chloride containing three drops of quinoline. The resultant clear solution was concentrated to a few ml. and the crystalline acid chloride was removed by filtration, washed with a small amount of dry ether; yield 1.6 g., (95%), m. p. 178–180° with decomposition.

Anal. Calcd. for $C_{11}H_9O_3N_2Cl$: Cl, 14.68. Found: Cl, 14.3.

The acyl chloride (IX) upon treatment with diazomethane gave a diazoketone which was judged to be identical with (III) on the basis of mixed melting point tests.

1-(or 3)-Methyl-2,4-quinazolinedione-5-carboxylic Acid (X).—Scott and Cohen reported that limited methylation of 2,4-quinazolinedione-5-carboxylic acid with dimethyl sulfate in the presence of sodium hydroxide yields 2,4-dimethoxyquinazoline-5-carboxylic acid. However, Lange, Chisholm and Szabo later claimed that the product was actually 1,3-dimethyl-2,4-quinazolinedione-5-carboxylic acid. The acid obtained after repeating the work in this Laboratory (after two recrystallizations from ethanol) was a monomethyl acid as shown by the analysis, m. p. 332–333° (uncor.).

Anal. Calcd. for $C_{10}H_8O_4N_2$: C, 54.54; H, 3.66; neut. equiv., 220. Found: C, 54.5; H, 3.85; neut. equiv., 221, 222.

5-(1-Hydroxyethyl)-1(or 3)-methyl-2,4-quinazolinedione (XII).—A suspension containing 1 g. (0.0034 mole) of 5-bromoacetyl-1(or 3)-methyl-2,4-quinazolinedione (IV) or 0.9 g. (0.0036 mole) of 5-diazoacetyl-1,3-dimethyl-2,4-quinazolinedione (III) and 10 ml. of a 10% stannous chloride solution in concentrated hydrochloric acid was heated on a water-bath with stirring for two hours. The resultant clear solution was diluted with 20 ml. of water and, after standing overnight, yielded 0.7 g. (95%), and 0.35 g. (45%) of colorless crystals melting at 212–213°.

Anal. Calcd. for $C_{11}H_{12}O_3N_2$: C, 59.97; H, 5.50; N, 12.72. Found: C, 59.8; H, 5.21; N, 12.9.

1-(or 3)-Methyl-2,4-quinazolinedione-5-carboxylic Acid (XI).—One gram (0.0039 mole) of 5-diazoacetyl-1,3-dimethyl-2,4-quinazolinedione (III) or 1.0 g. (0.0034 mole) of 5-bromoacetyl-1(or 3)-methyl-2,4-quinazolinedione (IV) or 0.51 g. (0.0023 mole) of 5-(1-hydroxyethyl)-1(or 3)-methyl-2,4-quinazolinedione (XII) was suspended in 50 ml. of a water solution containing 1.25 g. (0.008 mole) of potassium permanganate. The mixture was maintained at 80° with stirring for one hour. After removing the precipitated manganese dioxide, the clear, slightly colored solution was carefully acidified with dilute hydrochloric acid. The crystals which formed on cooling were separated, yielding 0.60 g. (66%), 0.40 g. (62%) and 0.14 g. (27%) of product, respectively. A portion of each was purified by decolorizing with carbon and recrystallizing twice from aqueous alcohol, m. p. 230–237° with evolution of gas.

Anal. Calcd. for $C_{10}H_8O_4N_2$: C, 54.53; H, 3.66; neut. equiv., 220. Found: C, 54.9; H, 3.83; neut. equiv., 218.

1(or 3)-Methyl-2,4-quinazolinedione (XIII).—Two and a half grams (0.011 mole) of 1(or 3)-methyl-2,4-quinazolinedione-5-carboxylic acid (XI) was heated to 250° in a sublimation apparatus. After the evolution of carbon dioxide ceased, the residue was sublimed at 200° under reduced pressure. The sublimate (0.70 g., 35%) was triturated with a small amount of 1% sodium carbonate solution and the insoluble residue recrystallized from ethanol; hard needles, m. p. 198–199°.

Anal. Calcd. for $C_9H_8O_2N_2$: C, 61.34; H, 4.58. Found: C, 61.2; H, 4.80.

Summary

Methods for the preparation of an amino alcohol derived from 2,4-quinazolinedione-5-carboxylic acid are given in detail. Several unusual reactions of 5-diazoacetyl-1,3-dimethyl-2,4-quinazolinedione are described. Evidence supporting the existence of two isomeric 1-methyl-2,4-quinazolinediones and two isomeric 3-methyl-2,4-quinazolinediones is presented.

CORVALLIS, OREGON RECEIVED AUGUST 21, 1948