[CONTRIBUTION FROM THE HAVEMEYER LABORATORIES OF COLUMBIA UNIVERSITY, No. 179.]

RESEARCHES ON QUINAZOLINES (TWENTY-FIFTH PAPER). THE SYNTHESIS OF 6- AND 7-AMINO-2-METHYL-4-QUINAZOLONES FROM 4- AND 5-ACETAMINOACETANTHRANILS.[1]

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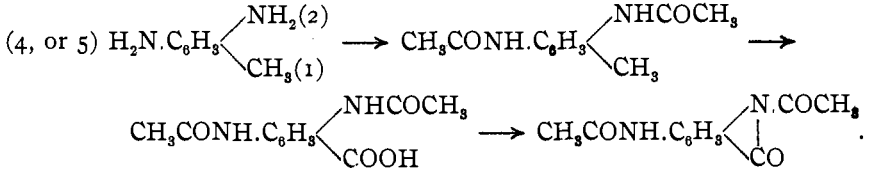
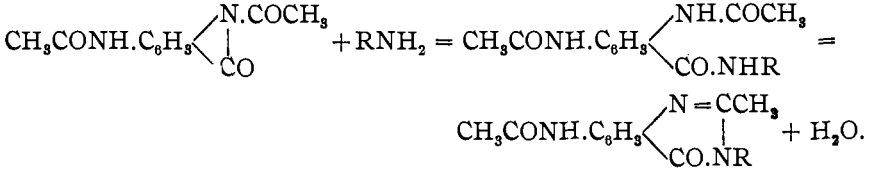
The 4- and 5-acetaminoacetanthranils were prepared from the corresponding diaminotoluenes by acetylating, oxidizing the acetyl derivatives with potassium permanganate in neutral solution, and treating the diacetamino acids with excess of acetic anhydride:



The oxidation of the 2,5-diacetaminotoluene proved much more troublesome than that of the 2,4-isomer, and the yield of diacetamino acid considerably less.

By condensing these anthranils with primary amines,[2] acetamino-4-quinazolones result:



On splitting off the acetyl group, the free 6- or 7-aminoquinazolones were obtained, from which in turn other derivatives were produced.

The amines used in the experiments were ammonia, methyl, ethyl, normal propyl, secondary butyl and isoamyl amines, aniline, *p*-anisidine, *p*-phenetidine, *p*-aminobenzonitrile, α-naphthylamine, hydrazine, phenylhydrazine, and 7-amino-2-methyl-4-quinazolone. Of these, the condensation with the secondary butylamine (2-aminobutane), for some unknown reason, stopped at the amide stage. The other amines all gave quinazolones.

Of the four possible Bz-monaminoquinazolines, the 5-amino derivatives have been described by Bogert and Chambers[3] and the 7-amino

[1] Read at the meeting of the New York Section, Jan. 7, 1910.

[2] Anschütz, Schmidt and Greiffenberg, *Ber.*, **35**, 3480 (1902); Bogert, *et al.*, THIS JOURNAL, **27**, 649, 1305, 1327; **28**, 94, 884, 1449; **29**, 82, 517, 729; etc.

[3] THIS JOURNAL, **28**, 208 (1906).

by Bogert and Klaber[1] and Bogert and Kropff.[2] Zacharias[3] prepared a crude 8-amino-2-methyl-4-quinazolone, by reduction of the corresponding nitro compound, but failed to get the substance pure.

The 6-amino derivatives described in the following pages are the first definitely shown to belong to this series. It seems likely that the aminoquinazolines prepared by Griess[4] and by Niementowski[5] carry the amino group at position 6, although this remains to be proven. The same is true of the diaminoquinazoline of Niementowski,[6] where it is quite probable that the two amino groups are located at 6 and 8, although their position likewise has yet to be determined.

On account of the greater expense of the 2,5-diaminotoluene, most of our experiments were carried out with the 2,4-isomer, and the majority of the products are therefore 7-aminoquinazolines.

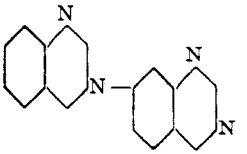
Practically all of the new products are crystalline solids of high melting or decomposing points. Some of the quinazolines are soluble in boiling water. Most of them are more or less soluble in alcohol and insoluble or difficultly soluble in ether. Those carrying the —CO.NH— $\rightleftharpoons$ —C(OH) : N— grouping dissolve in cold caustic alkalies and are reprecipitated from these solutions on saturation with carbon dioxide, but this grouping is not affected by acylating agents or by phenylhydrazine.

With chloroform and alcoholic caustic alkali, both 6- and 7-aminoquinazolones give off a faint not unpleasant odor when heated.

By the diazo reaction, the amino group can be replaced by other groups or, by diazotizing and combining with suitable couplers, azo dyestuffs may be produced.

The acetaminoquinazolones can be directly nitrated or brominated.

In former papers from this laboratory[7] we have shown that by condensing acylanthranils with hydrazine hydrate, or with 3-aminoquinazolones, 3,3′-diquinazolonyls may be obtained. We have now found that Bz-amino-4-quinazolones can be similarly condensed with acylanthranils, and in this way have obtained a 3,7′-diquinazolonyl, where the union of the two heterocycles is an N–C instead of an N–N one:



[1] THIS JOURNAL, **30**, 810 (1908).
[2] *Ibid.*, **31**, 1071 (1909).
[3] *J. prakt. Chem.*, (2) **43**, 443 (1891).
[4] *Ber.*, **2**, 416 (1869).
[5] *J. prakt. Chem.*, (2) **51**, 513 (1895).
[6] *Loc. cit.*
[7] Bogert and Seil, THIS JOURNAL, **28**, 884, *et al.*

In our study of the properties of 2-methyl-7-acetamino-3-amino-4-quinazolone, we were rather surprised to find that it failed to give the Bülow condensation[1] with diacetosuccinic ester.

Experimental.

I. Preparation of Anthranils.

4-Acetaminoacetanthranil, $(4)CH_3CONH \cdot C_6H_3\langle^{CO(1)}_{N.COCH_3(2)}$. — The 2,4-diaminotoluene was changed to the diacetaminotoluene by the action of acetic anhydride. The following was found to be the most rapid and satisfactory method of carrying out the acetylation:

Ten g. of the dry and finely pulverized diamine are added at once to about 20–25 g. pure acetic anhydride. An energetic reaction ensues, with considerable rise of temperature. As the reaction abates in violence, the rapidly thickening mass is stirred vigorously to insure complete contact with the anhydride. On cooling, the mass solidifies. The entire reaction is completed in a few minutes and without external heating. The product is washed thoroughly with water and then crystallized from the same, giving long, snowy, silky needles of the pure diacetaminotoluene.[2] From 30 g. pure diamine, we obtained 37.5–38.4 g. of the pure diacetyl derivative.

For most of our work, however, we used a crude commercial toluylenediamine, giving an acetylated product of darker color and in poorer yield. It was found unnecessary to purify this crude acetyl derivative, as the impurities were eliminated in the subsequent oxidation of the compound, and affected only the yield and not the purity of the oxidation product.

The 2,4-diacetaminotoluene was oxidized to the 2,4-diacetaminobenzoic acid by the action of potassium permanganate in neutral solution.[3] On the completion of the oxidation and concentration of the resulting solution of potassium diacetaminobenzoate, some unchanged diacetaminotoluene first separates and should be removed. On acidifying the filtrate, the acid precipitates in microcrystalline condition, sufficiently pure for the preparation of the acetanthranil. Starting with 20 g. of pure diacetaminotoluene, the yield of acid varied from 17.6–19.9 g. and half a gram of diacetaminotoluene was recovered unoxidized. With a like amount of the crude diacetaminotoluene, 2–3 g. remained unoxidized, and 15–16 g. of the acid were obtained.

In an attempt to nitrate this diacetaminobenzoic acid, it was treated with excess of fuming nitric acid at 35°. Most of the diacetamino acid dissolved, and on diluting the solution with water reprecipitated ap-

[1] *Ber.*, **39**, 2621, 3372 (1907), *et al.*

[2] Koch, *Ann.*, **153**, 132.

[3] Ullmann and Uzbachian, *Ber.*, **36**, 1803 (1903).

parently unchanged, for when washed with water and recrystallized from alcohol, fine, colorless needles resulted, of approximately the same melting point (261° cor.) and composition (found: N, 12.0; theory, 11.86) as the original acid.

Twenty to twenty-five g. acetic anhydride were heated to gentle boiling and 10 g. well-dried and finely pulverized diacetamino acid slowly stirred in, so that the solution remained fairly clear and gentle boiling continued. In this way, bumping is avoided. When the acid had all been added, the solution was concentrated to about half its original volume, and on cooling the mass solidified in rosettes of pale yellowish or colorless needles of the anthranil. Yield, somewhat over eight grams. Purified by crystallization from acetic anhydride, it forms colorless needles, m. p. 220° (cor.).

Found: N, 13.04. Calculated for $C_{11}H_{10}O_3N_2$: N, 12.90.

It is slightly tribo-electric. In presence of moisture, it is hydrated to the diacetamino acid. Heated with primary amines, it yields 7-acetamino-2-methyl-4-quinazolones.

2,5-Diacetaminobenzoic Acid, $(2,5)(CH_3CONH)_2C_6H_3.COOH$. — 2,5-Diacetaminotoluene[1] was prepared by adding the diaminotoluene hydrochloride to a solution of fused sodium acetate in acetic anhydride, the temperature of the solution being maintained above the boiling point of acetic acid, then boiling the solution for a few minutes. When cold, the mixture was diluted with water and the precipitated acetyl derivative recrystallized from water, in which it is much more soluble than the 2,4-isomer. Yield, 21 g. acetyl derivative from 30 g. of the diamine hydrochloride.

This acetyl derivative was oxidized with potassium permanganate in presence of magnesium sulphate. It is much more difficult to oxidize than the 2,4-isomer. From 10 g. of the diacetaminotoluene and 30 g. potassium permanganate (double the calculated amount), but 4 g. of the acid were obtained. A further increase in the amount of permanganate failed to increase the yield of acid. The acid precipitates usually in an amorphous state, but assumes a crystalline condition on standing. Treated with bone-black and recrystallized from alcohol, it forms minute, colorless crystals, melting with decomposition at 262° (cor.).

Found: N, 11.97. Calculated for $C_{11}H_{12}O_4N_2$: N, 11.86.

It is soluble in strong mineral acids and in aqueous solutions of caustic or carbonated alkalies, but is insoluble in dilute hydrochloric or in acetic acid. It dissolves also in nitrobenzene, aniline, or alcohol, but is not appreciably soluble in ether, carbon tetrachloride, ligroin or benzene.

[1] Nietzki, *Ber.*, 10, 1157 (1877); 12, 2237 (1879).

5-Acetaminoacetanthranil, $(5)CH_3CONH.C_6H_3\begin{cases}CO(1)\\ |\\ N.COCH_3(2)\end{cases}$. — Five grams of the diacetamino acid were added to 10 g. hot acetic anhydride and the solution boiled down to one-third its original bulk. On cooling, the anthranil separated in coarse, yellowish-brown needles, which, recrystallized twice from acetic anhydride, still retained a faint yellowish-brown cast and melted at 253° (cor.). Yield, 3.5 g. anthranil from 5 g. acid.

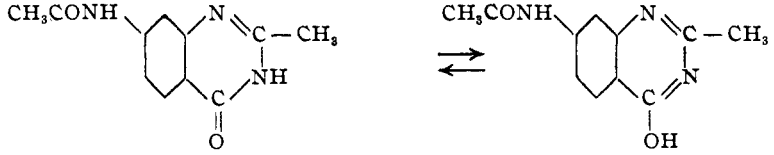
Found: N, 13.02. Calculated for $C_{11}H_{10}O_3N_2$: N, 12.90.

Like its isomer, this anthranil readily takes up moisture and reverts to the diacetamino acid. With primary amines, it yields 6-acetamino-2-methyl-4-quinazolones.

II. Quinazolones from 4-Acetaminoacetanthranil.

With the exception of the first compound, all the following quinazolines carrying the —CO.NH— $\rightleftharpoons$ —C(OH) : N— group are, for the sake of brevity, denominated quinazolones and given the —CO.NH— formula.

7-Acetamino-2-methyl-4-quinazolone (*7-Acetamino-2-methyl-4-hydroxyquinazoline*),



Eight g. 4-acetaminoacetanthranil were added to 50 cc. dilute ammonium hydroxide solution (10 cc. ammonium hydroxide solution of sp. gr. 0.9 to 40 cc. water) and the mixture heated a few minutes. The thick paste resulting was diluted with water to about 400 cc. and boiled for several minutes. Part dissolved and part separated (with more ammonia, a clear solution can be obtained, but the excess of ammonia must then be boiled off, or the separation of the product is not so complete). On cooling, the quinazolone separated form the solution in fine, short, silky, colorless needles, softening in the neighborhood of 342° and melting at 344° (cor.). Yield, 5.5 g.

Found: N, 19.53. Calculated for $C_{11}H_{11}O_2N_3$: N: H_2O, 19.35.

It is easily soluble in boiling water or in alcohol, slightly soluble in ethyl acetate, very difficultly soluble or insoluble in ether, carbon tetrachloride or toluene.

From water it crystallizes with water of crystallization: 1.0363 g. air-dried sample lost 0.15 g. on drying to constant weight at 100–10°.

Found: H_2O, 14.46. Calculated for $C_{11}H_{11}O_2N_3.2H_2O$: H_2O, 14.23.

7-Amino-2-methyl-4-quinazolone.—Five and one-half g. of the above acetyl derivative were boiled for about an hour with dilute potassium

hydroxide solution (5 g. KOH to 50 cc. water), the solution cooled, diluted, filtered, and the filtrate saturated with carbon dioxide. The aminoquinazolone separated in fine, silky, colorless hairs, rapidly assuming a faint pinkish cast on standing. It can be further purified by recrystallization from dilute alcohol. From water it crystallizes with half a molecule of water of crystallization:

Found: H_2O, 4.8. Calculated for $(C_9H_9ON_3)_2.H_2O$: H_2O, 4.9.

The anhydrous compound melts at 311° (cor.).

Found: C, 61.7 and 61.8; H, 5.1 and 5.2. Calculated for $C_9H_9ON_3$: C, 61.7; H, 5.1.

The substance is therefore identical with the 7-amino-2-methyl-4-quinazolone prepared by Bogert and Klaber[1] by reduction of the corresponding nitro compound.

It is tribo-electric, and gradually darkens on standing in the air. It is readily soluble in hot acetone, very slightly soluble in hot benzene, and apparently insoluble in ligroin. Boiled with alcoholic potassium hydroxide solution and chloroform, it emits an odor, presumably of an isonitrile, and yet of a rather pleasant banana-like character.

Bogert and Seil[2] found that when 5-nitro-2-methyl-3-amino-4-quinazolone was heated with phenylhydrazine, the 3-amino group was replaced by the phenylhydrazino group and the CO of the quinazolone reacted with a second molecule of the hydrazine, the result being a phenylhydrazinophenylhydrazone. A similar reaction did not occur when the above 7-amino-2-methyl-4-quinazolone and phenylhydrazine were heated together, alone or in alcoholic solution. No ammonia was evolved and the original quinazolone was recovered unaltered. It seems strange that the Bz-amino group failed to react, as an aromatic amino group can thus often be replaced directly by the phenylhydrazino group.

When the aminoquinazolone was boiled with formaldehyde and potassium cyanide, a reaction took place, but we failed to isolate any new products from the mixture. No change occurred when the aminoquinazolone was boiled with ethyl chloroacetate.

Azo dyestuffs can readily be produced from this amine by the usual diazotizing and coupling reactions.

Potassium Salt.—Square, colorless plates, easily soluble in cold water, but slightly soluble in alcohol.

Hydrochloride.—Prepared by the action of strong hydrochloric acid upon the free base or upon its ethyl acetate solution. Light brown, granular powder, decomposing on heating.

Chloroplatinate—Red, granular crystals.

Found: Pt, 25.6. Calculated for $(C_9H_{10}ON_3)_2PtCl_6$: Pt, 25.6.

[1] THIS JOURNAL, **30**, 810 (1908).

[2] *Ibid.*, **28**, 88 (1906).

Dinitro-7-acetamino-2-methyl-4-quinazolone. — The acetaminoquinazolone was added to a slight excess of fuming nitric acid at room temperature. It dissolved in the acid with a hissing sound and rise of temperature, and the solution finally set to a solid mass. Water was added and the temperature raised to boiling. During the boiling some decomposition was indicated by an escape of carbon dioxide. The solution on cooling deposited the nitro compound as a dark orange, sandy precipitate. After several recrystallizations from dilute acetic acid, it was obtained in orange, sandy crystals, melting with decomposition at about 302° (cor.). Yield, very poor.

Found: N, 22.9. Calculated for $C_{11}H_9O_6N_5$: N, 22.8.

It is soluble in boiling water, very slightly soluble in boiling alcohol, in ether or in nitrobenzene. In aqueous caustic alkalies, it dissolves to a dark orange solution, from which it is precipitated slowly by saturation with carbon dioxide, more rapidly by acidification with acetic acid. The positions of the nitro groups were not determined, but it seems most likely that they are 6 and 8.

Bromo-7-acetamino-2-methyl-4-quinazolone. — The acetaminoquinazolone was suspended in dilute (50 per cent.) acetic acid and the mixture warmed. Bromine was then added carefully to the warm solution. The reaction was vigorous, hydrobromic acid being evolved and the quinazolone dissolved. Soon thereafter the bromoquinazolone began crystallizing from the hot solution in minute needles. The solution was cooled, water added, the precipitate filtered out, washed, and recrystallized from dilute acetic acid or from a mixture of alcohol and acetic acid, in both of which it is rather difficultly soluble. It was thus obtained in minute needles, practically colorless, which began to darken at about 287° (cor.) and melted at 292° (cor.).

Found: N, 14.1; Br, 27.75. Calculated for $C_{11}H_{10}O_2N_3Br$: N, 14.2; Br, 27.03.

It is difficultly soluble in boiling alcohol. The use of a large excess of bromine in the above method of preparation gave the same product.

Bromo-7-amino-2-methyl-4-quinazolone. — The acetyl derivative just described was boiled for about an hour with ten per cent. potassium hydroxide solution, the solution cooled, diluted, filtered, and the filtrate saturated with carbon dioxide. The light yellow flocculent precipitate which separated was washed with water and purified by two crystallizations from alcohol. Light yellow flaky crystals were obtained, melting at 272–3° (cor.).

Found: N, 16.55. Calculated for $C_9H_8ON_3Br$: N, 16.53.

The substance is tribo-electric. It is moderately soluble in cold alcohol, easily in hot. It also dissolves in hot water, in warm nitrobenzene or isoamyl alcohol, but is apparently insoluble in ether, carbon tetra-

chloride or chloroform. The position of the bromine was not determined. Probably it is at 6.

7-Formamino-2-methyl-4-quinazolone, $HCONH.C_6H_3.CO.NH.C(CH_3) : N$. —7-Amino-2-methyl-4-quinazolone was boiled for four hours with excess of glacial formic acid, the excess of acid distilled off, the residual solution diluted, precipitated with sodium carbonate, and the precipitate crystallized from water. Colorless feathery crystals resulted, darkening at about 300°, softening in the neighborhood of 335°, and melting finally at 339–40° (cor.).

Found: N, 20.46. Calculated for $C_{10}H_9O_2N_3$: N, 20.69.

On standing a few days with ammoniacal silver nitrate solution to which a little sodium hydroxide has been added, it gives a silver mirror.

7-Propionamino-2-methyl-4-quinazolone, prepared in similar fashion, from the aminoquinazolone and propionic anhydride, crystallizes from water in long, white, silky needles, softening at about 317–20°, and melting at 326–7° (cor.).

Found: N, 18.48. Calculated for $C_{12}H_{13}O_2N_3$: N, 18.18.

It is tribo-electric and rather difficultly soluble in water or alcohol. In the latter solvent, it is much less soluble than the free aminoquinazolone. In hot, dilute organic acids, it is moderately soluble.

7-Hydroxy-2-methyl-4-quinazolone, $HO.C_6H_3.CO.NH.C(CH_3) : N$.—The 7-amino-2-methyl-4-quinazolone was dissolved in dilute hydrochloric acid and treated at 0° with the calculated amount of sodium nitrite in aqueous solution. Upon completion of the reaction, the mixture was diluted with water and boiled. Nitrogen was evolved freely and the color of the solution changed from yellow to orange. When the evolution of nitrogen ceased, the solution was allowed to cool. A small amount of flaky precipitate separated, but without removing this the mixture was neutralized with sodium carbonate. A voluminous yellow precipitate resulted. As we failed to get good crystals of this from any of the ordinary solvents, it was treated with moderately strong hydrochloric acid, which dissolved the greater part of it. The insoluble, dark orange portion was filtered out, and the filtrate neutralized with sodium carbonate. The light brown precipitate thus produced was again dissolved in hydrochloric acid, the solution filtered, and the filtrate reprecipitated with sodium carbonate. It was then dissolved in caustic alkali, yielding a red solution, reprecipitated with acetic acid, and dried. As thus purified, it formed a light brown powder, beginning to darken at about 345°, but not melting at that temperature.

Found: N, 16.28. Calculated for $C_9H_8O_2N_2$: N, 15.91.

It dissolves in hot alcohol or hot dilute acetic acid, but does not crystallize well from either solvent. It is soluble to a red solution in potassium hydroxide, and is reprecipitated from this solution by acetic acid but not by carbon dioxide. It is insoluble in ether, chloroform, carbon tetrachloride, benzene, toluene or acetone, but dissolves in hot isoamyl alcohol, aniline or nitrobenzene.

That portion of the original reaction product which was insoluble in the hydrochloric acid and dark orange in color, dissolved in potassium hydroxide solution with a red color, and when reprecipitated with hydrochloric acid came down in a gelatinous, colloidal condition which could not be further purified because of the small amount of material available.

7-Acetoxy-2-methyl-4-quinazolone, $CH_3COO.C_6H_3.CO.NH.C(CH_3) : N$.—On boiling the above 7-hydroxyquinazolone for an hour with excess of acetic anhydride, a reddish brown solution was obtained. This was cooled, diluted, and neutralized with sodium carbonate, giving a fine light brown precipitate which, on crystallization from alcohol, appeared in large pale brownish needles, softening at about 262° and melting at 266° (cor.).

Found:	C, 60.53;	H, 4.83;	N, 13.06.
Calculated for $C_{11}H_{10}O_3N_2$:	C, 60.55;	H, 4.60;	N, 12.84.

7-Cyano-2-methyl-4-quinazolone, $NC.C_6H_3.CO.NH.C(CH_3) : N$.—The 7-amino-2-methyl-4-quinazolone was diazotized and boiled with copper potassium cyanide solution. The precipitate was filtered out, washed with water, dried and extracted with carbon tetrachloride, to free it from metallic cyanides. On evaporating the carbon tetrachloride, a colorless crystalline mass remained, which was further purified by two crystallizations from alcohol, and then appeared in colorless feathery needles, melting at about 303–4° (cor.), and not volatile with steam.

Found: N, 22.0. Calculated for $C_{10}H_7ON_3$: N, 22.6.

The unsatisfactory character of this analytical result is due partly to the fact that the yield of product in the above reaction is very small and we did not have sufficient to run a good analysis. From 5 g. of the amino compound, the yield of pure cyano compound was only 0.1 g. This was particularly disappointing, as we had hoped to obtain sufficient to saponify to the corresponding acid, for the latter has already been described in a previous paper from this laboratory.[1]

7-Acetamino-2,3-dimethyl-4-quinazolone,

$CH_3CONH.C_6H_3.CO.N(CH_3).C(CH_3) : N$, was prepared from 4-acetamino acetanthranil in essentially the same manner as the monomethyl com-

[1] Bogert, Wiggin and Sinclair, THIS JOURNAL, 29, 87 (1907).

pound, using methylamine instead of ammonia. Recrystallized from alcohol, it forms colorless silky needles, melting at 284° (cor.).

Found: N, 18.5. Calculated for $C_{12}H_{13}O_2N_3$: N, 18.2.

It is soluble in hot water or in alcohol, slightly soluble in acetone, insoluble in ether, carbon tetrachloride or ligroin.

7-Amino-2,3-dimethyl-4-quinazolone.—The above acetyl derivative was heated for about an hour with 10 per cent. potassium hydroxide solution in excess, the solution filtered hot, and the filtrate allowed to cool. The free base separated as the filtrate cooled in rosettes of fine colorless silky needles (or short heavy prisms, if the cooling occurred very slowly), which darkened on exposure to the air, and on recrystallization from water melted at 224° (cor.).

Found: N, 22.36. Calculated for $C_{10}H_{11}ON_3$: N, 22.22.

The substance is easily soluble in warm water, alcohol or benzene, slightly soluble in chloroform, insoluble in ether or ligroin. On attempting, by means of the diazo reaction, to replace the amino group by an OH, the yield of product was so small that the effort was abandoned.

Chloroplatinate.—Red crystals.

Found: Pt, 24.6. Calculated for $(C_{10}H_{11}ON_3)_2PtCl_6$: Pt, 24.7.

7-Acetamino-2-methyl-3-ethyl-4-quinazolone. — 4-Acetaminoacetanthranil was heated with an aqueous ethylamine solution. The anthranil dissolved and, on cooling, the quinazolone separated in colorless, glistening, pearly plates. Recrystallized from alcohol, it formed short colorless needles, melting at 254° (cor.).

Found: N, 17.07. Calculated for $C_{13}H_{15}O_2N_3$: N, 17.14.

It crystallizes from water in clusters of long, colorless, silky needles, slightly soluble in cold, readily in warm alcohol.

*7-Acetamino-2-methyl-3-*n*-propyl-4-quinazolone.* — 4-Acetaminoacetanthranil was added to the *n*-propylamine diluted with a little water, and the mixture heated. The anthranil dissolved and, on cooling, the quinazolone precipitated in colorless, silky needles. Recrystallized from water, rosettes of needles were obtained, melting at 206–7° (cor.).

Found: N, 16.46. Calculated for $C_{14}H_{17}O_2N_3$: N, 16.22.

*2,4-Diacetamino-*sec.*butylbenzamide,* $(2,4)(CH_3CONH)_2C_6H_3CONHC_4H_9$. —No condensation could be effected with the anthranil and a dilute aqueous solution of secondary butylamine (2-aminobutane), but when the anthranil was boiled with the pure amine, colorless needles separated from the solution on cooling. These needles were purified by repeated crystallization from dilute alcohol, giving finally a m. p. of 235° (cor.). Dried at 100–20°, the substance was analyzed with the following result:

Found: N, 14.61. Calculated for the quinazolone ($C_{15}H_{19}O_2N_3$): N, 15.38; for the intermediate amide ($C_{15}H_{21}O_3N_3$): N, 14.43.

The product is thus apparently the amide and not the expected quin-

azolone. It forms short, colorless needles. Boiled with water, these crystals dissolve, but do not separate again as the solution cools. Treated with potassium hydroxide solution, acetanthranilic acid results and not the quinazolone.

7-Acetamino-2-methyl-3-isoamyl-4-quinazolone.—When 4-acetaminoacetanthranil was heated with a dilute aqueous solution of isoamylamine, no quinazolone was obtained. The anthranil was therefore added directly to the pure undiluted amine and the mixture heated. The anthranil dissolved, but nothing separated from the solution on cooling. It was then diluted and heated, and on cooling the quinazolone separated as a white, flaky precipitate. Recrystallized repeatedly from dilute alcohol, it was obtained in rosettes of colorless, silky, feathery needles, melting at 288° (cor.), soluble in alcohol, difficultly soluble in cold water, moderately soluble in hot.

Found: N, 14.76. Calculated for $C_{16}H_{21}O_2N_3$: N, 14.63.

7-Acetamino-2-methyl-3-phenyl-4-quinazolone was obtained by heating the anthranil and aniline together. Recrystallized from alcohol, it formed minute, colorless, pearly octahedra, melting at 276° (cor.).

Found: N, 14.24. Calculated for $C_{17}H_{15}O_2N_3$: N, 14.33.

It is apparently insoluble in ether, chloroform, acetone or water; very slightly soluble in hot carbon tetrachloride; but dissolves readily in hot alcohol or nitrobenzene.

*7-Acetamino-2-methyl-3-*p-*anisyl-4-quinazolone.*—1.09 g. of 4-acetaminoacetanthranil and 0.61 g. *p*-anisidine were intimately mixed and the mixture heated. At 55° it formed a thick paste, gradually growing more fluid up to 90° when the mass solidified. The temperature was then raised to 100° and the salmon-colored mass, after a short heating at this temperature, allowed to cool. Crystallized from dilute alcohol, flesh-colored, glistening octahedra were obtained, melting at 273° (cor.), easily soluble in hot alcohol, apparently insoluble in water, ether or chloroform.

Found: N, 13.2. Calculated for $C_{18}H_{17}O_3N_3$: N, 13.0.

*7-Acetamino-2-methyl-3-*p-*phenetyl-4-quinazolone.*—0.7 g. *p*-phenetidine was dissolved in dilute alcohol, 1 g. 4-acetaminoacetanthranil added, and the temperature raised to boiling. No condensation took place. But when the two substances were heated together dry at 95°, in the same proportion, the mixture first liquefied, then solidified (at about 80°). The crude product on crystallization from dilute alcohol gave clusters of fine short needles, of a slight pinkish cast, and melting at 259° (cor.).

Found: C, 67.50; H, 5.88; N, 12.66. Calculated for $C_{19}H_{19}O_3N_3$: C, 67.66; H, 5.64; N, 12.46.

It is difficultly soluble in hot water or in carbon tetrachloride, insoluble in ether, but dissolves in boiling benzene, and is easily soluble in warm

chloroform, ethyl or isoamyl alcohol. The structure of this compound recalls rather remotely that of phenacetine, but its physiological properties have not been studied.

4-Acetaminoacetanthranil and p-*Aminobenzonitrile.*—2.18 g. of the anthranil were heated with 1.18 g. of the nitrile. At 85° the mixture formed a thick paste, which became thinner as the temperature rose. At 140° the heating was interrupted and the melt allowed to cool. When the crude product was crystallized from dilute alcohol, rosettes of pale yellowish, downy needles were obtained, very strongly tribo-electric and softening at about 240°. Recrystallized until colorless, these needles melted at 258° (cor.) with decomposition.

Found: N, 13.36. Calculated for the quinazolone ($C_{18}H_{14}O_2N_4$): N, 17.61.

The product is evidently not the quinazolone. Dried three hours at 130–60° and again analyzed, the nitrogen percentage was found to be 13.41, *i. e.*, practically unchanged.

The substance is soluble in alcohol, insoluble in water. In dilute alcohol, it gives an opalescent solution. Boiled with dilute (10 per cent.) potassium hydroxide solution, it dissolves with copious evolution of ammonia, but no precipitate results when the solution is acidified with acetic or hydrochloric acid. Attempts to prepare an acetyl derivative were unsuccessful.

In another experiment, the constituents were heated to a somewhat higher temperature (170°), but the product showed the same melting point (258° cor.) and approximately the same nitrogen percentage (found, 12.96 per cent.).

7-Acetamino-2-methyl-3-α-naphthyl-4-quinazolone.—1.09 g. 4-acetamino acetanthranil and 0.715 g. α-naphthylamine were heated together. The mixture became pasty at about 50°, quite fluid at 80–100°, thickening again at 120°. The heating was carried to 150° and the melt then allowed to cool. When cold it was brittle and highly tribo-electric. Treated with cold chloroform, it dissolved and then light-colored flakes gradually separated. On warming, this precipitate increased. It was filtered from the warm solution, washed with ether and dried. The product is a pale gray powder, melting at 256° (cor.).

Found: N, 12.05. Calculated for $C_{21}H_{17}O_2N_3$: N, 12.24.

It appears to be less soluble in hot than in cold chloroform. It is soluble also in methyl or ethyl alcohol, or in glacial acetic acid, but insoluble in ether.

7-Acetamino-2-methyl-3-amino-4-quinazolone.—On mixing 4-aetaɔmino-acetanthranil and hydrazine hydrate in equimolecular proportion and heating the mixture to boiling, the anthranil dissolved, and soon there separated from the boiling solution fine, colorless, glistening needles

which, when recrystallized from 95 per cent. alcohol, carry a molecule of water of crystallization, the anhydrous base melting at 268° (cor.).

Found: H_2O, 7.31. Calculated for $C_{11}H_{12}O_2N_4.H_2O$: H_2O, 7.2
Found: N, 24.38. Calculated for $C_{11}H_{12}O_2N_4$: N, 24.14.

The water of crystallization is not easily driven out at 110°, but can be removed by drying at 125–30°. The anhydrous base is practically insoluble in ether, benzene, water or cold alcohol; difficultly soluble in chloroform; moderately soluble in hot, dilute alcohol; easily soluble in warm nitrobenzene.

When an equimolecular mixture of the above quinazolone and diacetosuccinic ester, dissolved in glacial acetic acid, was boiled for an hour, no condensation occurred. When a little acetic anhydride was added to the glacial acetic acid solution, the only effect was acetylation of the amino group. The two substances were therefore fused together without solvent. A brown paste resulted at about 210°, considerable acetic acid being evolved during the fusion. When cold, the mass was pulverized, and the tan-colored product crystallized thrice from alcohol, giving short, tan-colored needles, melting at 253–4° (cor.) which, on further purification, proved to be only the unchanged quinazolone. The reaction therefore involved only the breaking down of the diacetosuccinic ester and no condensation to a pyrrole derivative. We had expected, from the investigations of Bülow[1] and our own experience with —N — NH_2 quinazolones, to get the pyrrole compound.

Hydrochloride.—The aminoacetaminoquinazolone was suspended in ether and the solvent saturated with dry hydrogen chloride. The free base was thus changed to the hydrochloride and remained insoluble in the ether. It was filtered out, washed with ether, and dried *in vacuo* over potassium hydroxide.

Found: N, 19.65. Calculated for $2C_{11}H_{12}O_2N_4.3HCl$: N, 19.53.

Short, colorless needles, darkening somewhat at about 305°, and melting with vigorous decomposition at 312° (cor.).

When the aminoquinazolone was dissolved in 95 per cent. alcohol and the solution saturated with dry hydrogen chloride, no hydrochloride was formed, the unchanged quinazolone itself precipitating.

2,4-Diacetaminobenzohydrazide, $(2,4)(CH_3CONH)_2C_6H_3CONHNH_2$.—In the interaction of the acetaminoacetanthranil and hydrazine hydrate (in 50 per cent. aqueous solution), if the anthranil is added to the hydrazine hydrate solution without heating, it remains in suspension for a few seconds, then heat is evolved and finally a snowy pasty mass is formed made of fine short needles. If water be now added and the mixture boiled, the aminoacetaminoquinazolone described above is formed.

[1] *Ber.*, **39**, 2621, 3372 (1906), etc.

If, on the other hand, these first crystals be filtered out, recrystallized from alcohol, and dried at 80°, the hydrazide is the product.

Found: N, 22.43. Calculated for $C_{11}H_{14}O_3N_4$: N, 22.4.

Dried six hours at 120–40°, no loss of weight occurred and no important change in the nitrogen percentage (found, 22.55 per cent. nitrogen). The crystals melt at the same point as the 7-acetamino-2-methyl-3-amino-4-quinazolone, probably passing into this by loss of water at higher temperatures.

3,7-Diacetamino-2-methyl-4-quinazolone, prepared from the aminoacetaminoquinazolone by the action of acetic anhydride, crystallizes from water with water of crystallization. These hydrated crystals melt down at 100°. From alcohol, it crystallizes in minute, colorless crystals, melting at 304° (cor.).

Found: N, 20.34 and 20.44. Calculated for $C_{13}H_{14}O_3N_4$: N, 20.44.

Excess of acetic anhydride causes no further acetylation.

3,7 - Diamino-2-methyl-4-quinazolone. — 7-Acetamino-2-methyl-3-amino-4-quinazolone was boiled for half an hour with dilute (10 per cent.) potassium hydroxide solution. On cooling, colorless, silky needles were deposited in clusters in such amount that the whole mass solidified. These crystals were washed with water and recrystallized from dilute alcohol, melting then at 238° (cor.).

Found: N, 29.7. Calculated for $C_9H_{10}ON_4$: N, 29.5.

7-Acetamino-2-methyl-3-anilino-4-quinazolone,

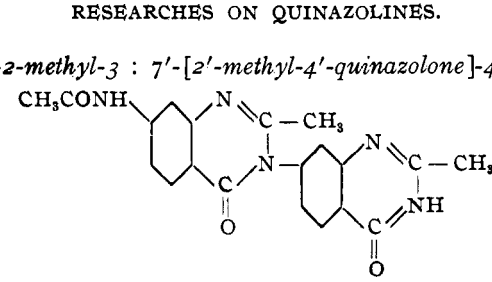
$CH_3CONH.C_6H_3.CO.N(NHC_6H_5).C(CH_3):N$. — 4 - Acetaminoacetanthranil was added to an equimolecular amount of phenylhydrazine in alcoholic solution and the mixture heated to boiling. A clear yellow solution resulted which gradually changed to dark red on continuing the heating. After a half hour's boiling, the solution was concentrated and allowed to cool. Nodules of fine yellow needles were deposited. After several recrystallizations from alcohol, they appeared as colorless, feathery needles, softening at about 208°, and melting at 214° (cor.).

Found: N, 18.4. Calculated for $C_{17}H_{16}O_2N_4$: N, 18.2.

The substance is soluble in hot water, benzene, chloroform, acetone, ethyl or isoamyl alcohol, or in nitrobenzene, less readily in ether or in carbon tetrachloride.

When the anthranil was added to a slight excess of pure and undiluted phenylhydrazine and the mixture gently warmed, the anthranil dissolved and the reaction proceeded with violent ebullition even when the source of external heating was immediately removed at the beginning of the reaction. It is likely that deeper-seated changes accompanied this reaction, as we failed to isolate any of the above anilino derivative among the products.

7-Acetamino-2-methyl-3 : 7'-[2'-methyl-4'-quinazolone]-4-quinazolone,



7-Amino-2-methyl-4-quinazolone and 4-acetaminoacetanthranil, in equimolecular proportion, were intimately mixed and the mixture heated gradually to 250°. The melt on cooling formed a brown, porous, brittle mass, giving a yellow powder when pulverized. This powder was dissolved in alcohol, the solution treated with bone-black twice, and the filtrate then concentrated. Short, thick, light yellow needles crystallized out, darkening at about 330° and melting at 335° (cor.).

Found: C, 63.86; H, 4.86; N, 18.61. Calculated for $C_{20}H_{17}O_3N_5$: C, 64.00; H, 4.53; N, 18.67.

The compound dissolves in boiling water, in alcohol or in nitrobenzene. It is very slightly soluble in carbon tetrachloride, benzene, ligroin or ether, but somewhat soluble in acetone. It dissolves also in potassium hydroxide solutions and is reprecipitated therefrom by saturation with carbon dioxide. The alcoholic solution of the substance shows a greenish fluorescence.

III. Quinazolones from 5-Acetaminoacetanthranil.

6-Acetamino-2-methyl-4-quinazolone, prepared from the 5-acetamino acetanthranil and ammonia, is much less readily soluble in alcohol than the 7-acetamino isomer. It crystallizes from this solvent in clusters of small, coarse, colorless needles or prisms, melting at 350° (cor.).

Found: N, 19.33. Calculated for $C_{11}H_{11}O_2N_3$: N, 19.35.

6-Amino-2-methyl-4-quinazolone.—The acetyl derivative was boiled with excess of 10 per cent. potassium hydroxide solution, and the solution then precipitated by carbon dioxide. The precipitate crystallized from water in rosettes of long, colorless, highly refracting needles, which began to darken in the neighborhood of 300°, softened somewhat at about 304°, and melted finally at 314–5° (cor.).

Found: N, 23.92. Calculated for $C_9H_9ON_3$: N, 24.0.

At 70–80°, the crystals lose their luster, although they do not carry any water of crystallization. The compound tends to darken on standing. It is insoluble or difficultly soluble in ether, ligroin, chloroform or benzene, but dissolves in ethyl or isoamyl alcohol, acetone or nitrobenzene.

6-Acetamino-2,3-dimethyl-4-quinazolone. — 5-Acetaminoacetanthranil was added to a dilute aqueous solution of methylamine and the mixture

heated. The anthranil first dissolved and then the quinazolone separated from the hot solution in colorless, silky needles, soluble in alcohol, and melting at 278° (cor.).

Found: N, 18.22. Calculated for $C_{12}H_{13}O_2N_3$: N, 18.18.

6-Acetamino-2-methyl-3-ethyl-4-quinazolone was prepared similarly, using ethylamine instead of methylamine. When the anthranil and ethylamine were heated together (the latter being used in aqueous solution), a clear solution was obtained, from which nothing separated on further heating or on cooling. A small amount of potassium hydroxide was added, the solution again boiled, and on long standing the quinazolone finely separated in long, colorless, silky needles which, after recrystallization from water, melted at 229° (cor.).

Found: N, 17.43. Calculated for $C_{13}H_{15}O_2N_3$: N, 17.14.

The crystals are highly refracting, and dissolve in hot water or in alcohol.

6-Acetamino-2-methyl-3-n-propyl-4-quinazolone, from the anthranil and *n*-propylamine, crystallizes from water in long, colorless, silky needles, melting at 181° (cor.).

Found: N, 16.45. Calculated for $C_{14}H_{17}O_2N_3$: N, 16.22.

6-Acetamino-2-methyl-3-phenyl-4-quinazolone.—The anthranil and pure aniline were heated together at 110°, and the product purified by repeated crystallization from dilute alcohol. It forms brownish plates, melting at 255° (cor.), very difficultly soluble in boiling water, readily in hot alcohol.

Found: N, 14.43. Calculated for $C_{17}H_{15}O_2N_3$: N, 14.33.

6-Acetamino-2-methyl-3-amino-4-quinazolone.—The anthranil was added to a dilute aqueous hydrazine hydrate solution and the mixture heated to boiling. The anthranil dissolved and, on cooling, the quinazolone crystallized out in rosettes of colorless, silky needles, which were washed with water and recrystallized from it, when they melted at 262–3° (cor.). The crystals are soluble in hot water or in alcohol.

Found: N, 24.29. Calculated for $C_{11}H_{12}O_2N_4$: N, 24.14.

ORGANIC LABORATORY, HAVEMEYER HALL,
COLUMBIA UNIVERSITY, June, 1910.

ETHYL TANNATE.

BY R. J. MANNING.

Received June, 1910.

Of the naturally occurring tannins gallotannic acid, obtained from gallnuts and many other sources, is the most important and best known. Strecker[1] claims that gallotannic acid is a glucoside of gallic acid as it yielded gallic acid and glucose on hydrolysis. Schiff[2] synthesized di-

[1] *Ann.*, **90**, 340.

[2] *Ibid.*, **170**, 49.