being soon recognized. Soxhlet especially devoted much of his time to the study of the method and established[1] the exact conditions under which the determination must be carried out in order to get satisfactory results.

BUREAU OF CHEMISTRY, WASHINGTON, D. C.

A REVIEW OF SOME RECENT INVESTIGATIONS IN THE QUINAZOLINE GROUP.[2]

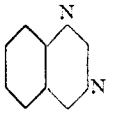
BY MARSTON TAYLOR BOGERT.

Received March 31, 1910.

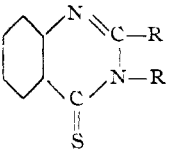
For several years past, the Organic Laboratory of Columbia University has been engaged in the synthesis and study of compounds belonging to that group of organic heterocycles known as quinazolines or phenmiazines.

To us, the work has been most interesting and enjoyable. The compounds obtained have been generally crystalline solids, quite readily purified, stable, and very satisfactory to work with.

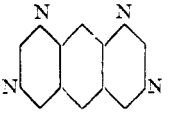
Our investigations have included—A. Quinazolines, B. Thioquinazolines, and C. Naphthotetrazines of quinazoline structure:



(Quinazoline)



(Thioquinazoline)



(1,3,7,9-Naphthotetrazine)

Incidentally, a great many new preparatory, intermediate and subsidiary products have been obtained. From the standpoint of new substances, the field has been an unusually fruitful one.

It is, therefore, not only an honor but also a pleasure to present on this occasion a brief synopsis of the major lines of the work to date.

A. Quinazolines.

Colby and Dodge,[3] as the result of their investigations of the interaction of nitriles and organic acids, under conditions of heat and pressure, came to the following conclusions:

I. Fatty nitriles and aromatic acids give fatty acids and aromatic nitriles.

II. Aromatic nitriles and fatty acids give mixed secondary amides.

III. Aromatic nitriles and aromatic acids give secondary amides, unless the temperature is very high, when the nitrile of the higher radical may form.

Mathews,[4] in continuation of this work, heated acetonitrile and anthranilic acid together under pressure, hoping thereby to obtain the

[1] *Z. anal. Chem.*, 18; 20, 425. For other references to modern investigators see standard text-books.

[2] Address at the Twentieth Anniversary Celebration of Clark University, Worcester, Mass., Sept. 14, 1909.

[3] *Am. Chem. J.*, 13, 1 (1891).

[4] THIS JOURNAL, 20, 654 (1898).

anthranilic nitrile. On examining the contents of the tube, he found not the nitrile desired but a colorless crystalline compound, melting at 232° (uncor.), which was not identified at the time.

Later, Bogert and Gotthelf[1] made a more careful study of this reaction and found that the crystalline substance melting at 232° was identical with the 2-methyl-4-ketodihydroquinazoline first described by Weddige,[2] and later obtained by Bischler and Burkart,[3] Bischler and Lang,[4] and Niementovskii.[5] By varying the nitrile, they obtained other quinazolines of analogous structure.

Continuing this work, Gotthelf[6] heated anthranilic acid under pressure with a:

IV. Fatty nitrile alone (using aceto-, propio-, *n*-butyro-, *i*-valero- and *i*-capronitriles).

V. Fatty nitrile and the corresponding fatty acid (acetonitrile and acetic acid, propionitrile and propionic acid, etc.).

VI. Fatty nitrile and a higher fatty acid (acetonitrile and propionic acid, *n*-butyronitrile and capric acid, etc.).

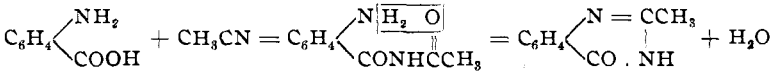
VII. Fatty nitrile and a lower fatty acid (isocapronitrile and propionic acid, etc.).

VIII. Fatty nitrile and the corresponding acid anhydride (propionitrile and propionic anhydride, valeronitrile and valeric anhydride, etc.).

IX. Fatty nitrile and higher acid anhydride (acetonitrile and propionic anhydride, etc.).

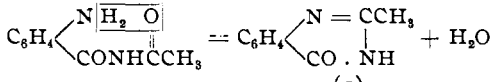
X. Fatty nitrile and lower acid anhydride (acetonitrile and formic acid, etc.).

In considering case IV, Bogert and Gotthelf at the time thought it probable that the production of a quinazoline was due to the formation of an intermediate secondary amide,



just as acetonitrile and acetic acid when heated under pressure give diacetoamide.[7]

One objection to this explanation of the course of the reaction lies in the fact that it involves a lactam condensation, whereas Weddige's investigations in this very field have made it quite clear that these condensations follow preferably the lactim course. If the intermediate secondary amide assumed by us passes directly into the quinazoline by loss of water, two different quinazolines should result according to whether the condensation is of lactam or lactim type:



(*a*)

[1] THIS JOURNAL, **22**, 129 (1900).

[2] *J. prakt. Chem.*, [2] **31**, 124 (1885).

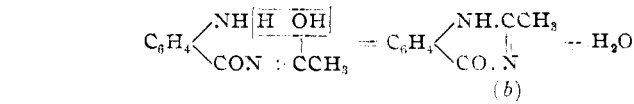
[3] *Ber.*, **26**, 1350 (1893).

[4] *Ibid.*, **28**, 282 (1895).

[5] *J. prakt. Chem.*, [2] **51**, 564 (1895) and *Ber.*, **29**, 1360 (1896).

[6] THIS JOURNAL, **23**, 611 (1901).

[7] Kekulé, *Lehrbuch* (1st ed.), **1**, 574; Gautier, *Ztschr. Chem.*, **1869**, 127.

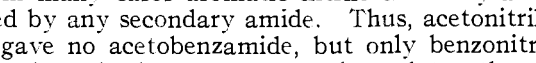


(*b*)

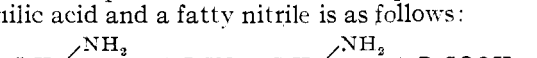
As a matter of fact, the product obtained by us is identical with (*a*).

Another objection is that it is not in harmony with the conclusions of Colby and Dodge[1] cited above. According to their experiments, the first products of the action of a fatty nitrile upon an aromatic acid at high temperature and pressure are the aromatic nitrile and the fatty acid, which may and often do subsequently combine to a mixed secondary amide. That the secondary amide is not the first product seems established by their results, for in no case where a fatty nitrile acted upon an aromatic acid was the secondary amide found unaccompanied by aromatic nitrile, while in many cases aromatic nitrile and fatty acids were found unaccompanied by any secondary amide. Thus, acetonitrile and benzoic acid at 220° gave no acetobenzamide, but only benzonitrile and acetic acid, whereas when the latter two were heated together at 220°, only acetobenzamide was formed.

It therefore seems probable that the first phase of the reaction between anthranilic acid and a fatty nitrile is as follows:



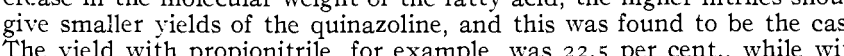
As aniline when heated to sufficiently high temperatures with fatty acids yields the corresponding anilides,[2] the second phase of the reaction is probably



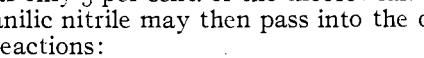
As the ease with which this acylation takes place decreases with increase in the molecular weight of the fatty acid, the higher nitriles should give smaller yields of the quinazoline, and this was found to be the case. The yield with propionitrile, for example, was 22.5 per cent., while with valeronitrile it was only 5 per cent. of the theoretical.

The acylanthranilic nitrile may then pass into the quinazoline by either of the following reactions:

or



That a simple molecular rearrangement of the acylanthranilic nitrile occurs,



seems unlikely, for the reason that when acetoanthranilic nitrile was heated for some time above its melting point, or when its solution in dry toluene was heated to high temperatures in sealed tubes, no change

[1] *Loc. cit.*

[2] Williams, *Ann.*, **131**, 288; Pebal, *Ibid.*, 91, 152.

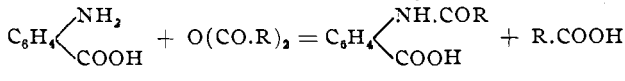
whatever occurred.[1] Moisture was, of course, rigidly excluded in these experiments, since a small amount of water, by successive addition and splitting off, would suffice to convert an indefinite amount of the nitrile to the quinazoline.

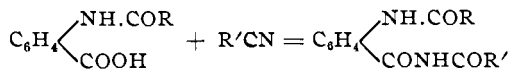
In further support of the assumption that the acylanthranilic nitrile is an intermediate product, are the following facts: (1) Acetanilide is found as a by-product in the tubes.[2] (2) The presence of a small amount of acetic anhydride greatly increases the yield of quinazoline. (3) The same quinazoline results when acetoanthranilic acid is heated in a sealed tube with acetonitrile as when anthranilic acid itself is used.[3] (4) Acetoanthranilic nitrile on partial hydrolysis changes immediately to the quinazoline.[4]

The by-products observed in the experiments were carbon dioxide, aniline, anilides, amides and ammonia. Of these, carbon dioxide and aniline are normal decomposition products of anthranilic acid at high temperatures. Partial hydrolysis of the nitrile accounts for the presence of amide. Aniline acting on the latter,[5] or upon the fatty acid present, yields the anilide, the by-product in the former case being ammonia.

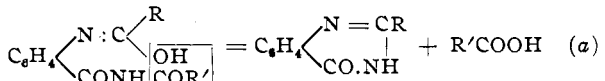
In those cases (V, VI and VII) where the anthranilic acid was heated with both the fatty nitrile and the fatty acid, the results are confusing and the interpretation obscure. Quinazolines were formed, but the course of the reactions is not clear and additional work is needed before any satisfactory conclusions can be reached.

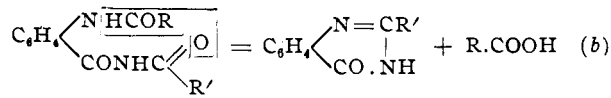
When an acid anhydride was added to the tubes containing the anthranilic acid and fatty nitrile (VIII, IX and X), the anhydride used determined the quinazoline formed in practically every case. In these experiments, the reaction is therefore probably as follows:





the latter then condensing in either of the following ways:





The nitrile was used with the corresponding acid anhydride (VIII), with a higher acid anhydride (IX), and with a lower anhydride (X). Of these, types VIII and IX invariably yielded pure quinazolines according to reaction (*a*) above. Only when a lower anhydride was used with the

[1] Bogert and Hand, THIS JOURNAL, **24**, 1034 (1902).

[2] Bogert and Gotthelf, *Ibid.*, **22**, 528 (1900).

[3] Bogert and Gotthelf, *Loc. cit.*

[4] Bogert and Hand, *Loc. cit.*

[5] Kelbe, *Ber.*, **16**, 1200 (1883).

nitrile (X), were products encountered which were mixtures of quinazolines.

Of these different sealed-tube reactions, much the best was that in which the anthranilic acid was heated with the fatty nitrile and the corresponding acid anhydride (VIII). The yield by this process was fair (30 to 50 per cent. of the theory) and, unless the heating was too high, the tube contents were invariably light-colored and crystalline.

In the foregoing, it is assumed that the secondary amide is an intermediate product in the formation of the quinazoline. Such an amide, R.CO.NH.CO.R′, being symmetrical, should be producible either from R.COOH and R′CN, or from R′COOH and RCN. In other words, since the formation of the -—CO.NH.CO— group is due solely to the combination of the CN and COOH, it should make no difference which radical carries the CN and which the COOH. The same secondary amide and, therefore, the same quinazoline, should result whether the acylanthranilic acid is heated with the fatty nitrile, or the acylanthranilic nitrile with the fatty acid (or its anhydride). On testing this practically,[1] such was indeed found to be the case, and a number of quinazolines were thus obtained from the acylanthranilic nitriles by heating them in sealed tubes with the fatty acid or, better, its anhydride.

In experimenting with these acylanthranilic nitriles, a method of converting them into the quinazolines, far superior to any of the methods described above, was discovered. It consists in digesting the acylanthranilic nitrile for a few minutes with a warm alkaline dioxide solution, and is really a beautiful method, being very rapid, simplicity itself in execution, and giving large yields of practically pure quinazolines. It depends upon the hydrolysis of the nitrile to the amide, the acylanthranilamide then condensing to the quinazoline, as shown by Weddige.[2]

In those cases where the *o*-amino acid is best obtained from its nitrile by saponification, it is convenient to be able to pass direct from the nitrile to the quinazoline. Thus, homoanthranilic nitrile is readily prepared from *m*-nitro-*p*-toluidine, through *m*-nitro-*p*-toluonitrile, and from the acyl derivatives of this homoanthranilic nitrile and an alkaline dioxide solution (hydrogen dioxide solution made alkaline with sodium hydroxide), the 7-methyl-4-quinazolones were prepared.[3]

By a number of different processes, including those already mentioned, starting with brominated anthranilic acids, bromoquinazolines were prepared.[4]

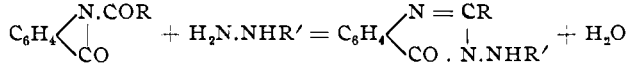
Our attention was next turned to the nitroquinazolines, and many were made from nitroanthranilic acids by the methods already described, and also by heating the ammonium salt of the nitroanthranilic acid with formamide,[5] by the direct action of heat on the ammonium salts of nitroacylanthranilic acids,[6] and by the action of primary amines on nitroacetoanthranils.[7] The last is a very fine method indeed, and one we have developed quite extensively.

[1] Bogert and Hand, THIS JOURNAL, **24**, 1031 (1902).
[2] *J. prakt. Chem.*, [2] **31**, 124 (1885); **36**, 141 (1887).
[3] Bogert and Hoffman, THIS JOURNAL, **27**, 1293 (1905).
[4] Bogert and Hand, *Ibid.*, **25**, 943 (1903); **28**, 94 (1906).
[5] Niementovskii, *J. prakt. Chem.*, [2] **51**, 564 (1895).
[6] Bischler and Burkart, *Ber.*, **26**, 1349 (1893).
[7] Anschütz, Schmidt and Greiffenberg, *Ber.*, **35**, 3480 (1902).

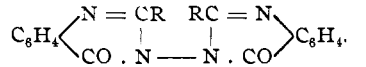
By these various methods, we prepared 5-nitro-,[1] 6-nitro-,[2] and 7-nitro-4-quinazolones.[3] Of the four possible types of benzoylnitroquinazolines, representatives of the 6-nitro,[4] and 8-nitro,[5] were already known. The preparation of the 5- and 7-nitro derivatives completed the series.

Reduction of the nitroquinazolines yielded the corresponding benzoylaminoquinazolines,[6] in which, as might have been expected, the amino group shows the usual aniline reactions.

Aminoquinazolines with the amino group on the miazine side of the nucleus were produced by condensing simple or substituted acylanthranils with primary hydrazines,[7]



With hydrazine itself, it was also found possible to condense two molecules of the anthranil with one of the hydrazine, thereby giving 3,3′-diquinazolonyls,



The same result can be accomplished, though less satisfactorily, by condensing the 3-aminoquinazoline with a second molecule of the anthranil. The di-quinazolonyls so far isolated are all very difficultly soluble and inert.

The 3-aminoquinazolines proved interesting because of their unsymmetrical secondary hydrazine structure, $>N.NH_2$. In the main, their properties coincide with those of other N-amino heterocyclic compounds. Thus, nitrous acid does not diazotize the amino group, but replaces it by hydrogen; with diacetosuccinic esters, they often yield pyrrole derivatives;[8] with aromatic nitroso bodies, they do not give azo compounds; nor are they oxidized to tetrazones by mercuric oxide. On the other hand, they do not usually condense with ketones, while they do occasionally yield phenyluramino derivatives with phenyl isocyanate.[9] In the elimination of the N-amino group by the action of nitrous acid, there must be some unstable intermediate product formed, for if immediately after the addition of the nitrous acid the mixture be poured into an alkaline solution of alpha- or beta- naphthol, dyestuffs are formed of considerable tinctorial power, the structure of which has not been elucidated.

Further experimentation with the acylanthranils showed that they

[1] Bogert and Chambers, THIS JOURNAL, **27**, 649 (1905); Bogert and Seil, *Ibid.*, **27**, 1305 (1905) and **29**, 532 (1907).

[2] Bogert and Cooke, *Ibid.*, **28**, 1449 (1906).

[3] Bogert and Steiner, *Ibid.*, **27**, 1327 (1905); Bogert and Seil, *Ibid.*, **29**, 532 (1907); Bogert and Klaber, *Ibid.*, **30**, 807 (1908).

[4] Dehoff, *J. prakt. Chem.*, [2] **42**, 347 (1890); Thieme, *Ibid.*, **43**, 441 (1891).

[5] Zacharias, *Ibid.*, **43**, 441 (1891).

[6] Bogert and Chambers, THIS JOURNAL, **28**, 207 (1906); Bogert and Klaber, *Ibid.*, **30**, 807 (1908).

[7] Bogert and Seil, *Ibid.*, **28**, 884 (1906); Bogert and Cook, *Loc. cit.*; Bogert and Klaber, *Loc. cit.*

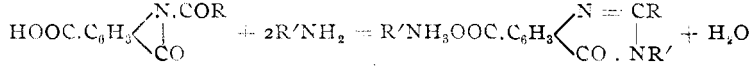
[8] Bülow, *Ber.*, **35**, 4312 (1902); **39**, 2621 and 3372 (1906).

[9] Bogert and Gortner, THIS JOURNAL, **31**, 943 (1909).

could also be condensed with amino nitriles or amino esters to the corresponding quinazolines.[1]

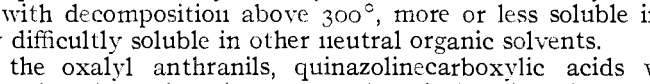
The ease with which acylanthranils condense with primary amines to crystalline quinazolines suggests the utilization of this reaction for the separation and identification of easily soluble or sirupy amines difficult to handle otherwise.

The same reaction was employed for the preparation of quinazoline carboxylic acids from acylanthranil carboxylic acids,[2]

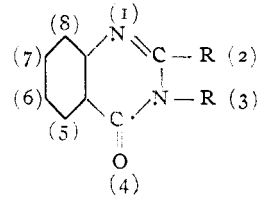


These quinazoline benzoylcarboxylic acids are colorless crystalline solids, melting with decomposition above 300°, more or less soluble in alcohol, but very difficultly soluble in other neutral organic solvents.

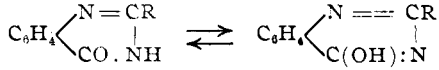
From the oxalyl anthranils, quinazolinecarboxylic acids were prepared carrying the carboxyl group on the miazine side of the nucleus,[3]



The particular quinazolines described in the foregoing are for the most part of the type designated as 4-ketodihydroquinazolines or, more simply, 4-quinazolones,



When there is an H at position 3 instead of a radical, there arises the possibility of keto-enolic tautomerism,



(4-Quinazolone) (4-Hydroxyquinazoline)

All those 4-quinazolones (4-hydroxyquinazolines) which carry a hydrogen at position 3 are easily soluble in aqueous solutions of the caustic alkalies and re-precipitable from such solutions by carbon dioxide or acetic acid. When these alkali salts are treated with alkyl halides, the 3-(*N*)alkyl derivative is the chief product.[4] The nitro derivatives furnish an apparent exception to this, in that the product with the higher alkyl halides is reported as chiefly the oxygen ether (*i. e.*, the 4-(*O*)alkyl, or -OR compound).[5] We are somewhat skeptical, however, of the accuracy of these results and feel that they should not be fully accepted until the pure oxygen ethers have been prepared by other processes and the two

[1] Bogert and Klaber, *Loc. cit.*

[2] Bogert, Wiggin and Sinclair, THIS JOURNAL, **29**, 82 (1907); Bogert and Jouard, *Ibid.*, **31**,489 (1909).

[3] Bogert and Gortner, *Ibid.*, **32**, 119 (1910).

[4] Bogert and May, *Ibid.*, **31**, 507 (1909).

[5] Bogert and Seil, *Ibid.*, **29**, 517 (1907).

products compared. One reason for this skepticism on our part is that certain of these supposititious oxygen ethers could not be hydrolyzed with concentrated mineral acids (hydrochloric), a result contrary to our experience and to that of others working with true oxygen ethers.

Pure 3-(*N*)alkyl derivatives are easily obtained by the acylanthranil reaction already described. For the isomeric 4-OR derivatives, the best method appears to be the treatment of the 4-chloroquinazolines with sodium alcoholates.[1] In the case of the simple alkyl derivatives of unsubstituted 4-quinazolones (4-hydroxyquinazolines), the (3)-NR compounds are colorless, odorless solids, quite soluble in water, generally very difficultly volatile with steam, of higher melting point than the 4-OR isomers, and are not hydrolyzed by strong hydrochloric acid. On the other hand, the 4-OR compounds are oily liquids or low-melting solids, usually of pleasant odor, readily volatile with steam, less soluble in water but more soluble in hydrochloric acid than the NR isomers, and are readily hydrolyzed by mineral acids to the hydroxyquinazoline (4-quinazolone) again. Some of the lower ones can even be distilled undecomposed at ordinary pressure.

In the preparation of the 4-chloroquinazolines from the 4-hydroxyquinazolines (4-quinazolones),[1] a methyl or ethyl group in position 2 exerts a peculiar influence upon the course of the reaction with phosphorus halides or similar halogenating reagents. In all such cases, it was found impossible to replace the OH at 4 by chlorine without simultaneously introducing three chlorine atoms in the benzene part of the nucleus. Even when 2,3-dimethyl-4-quinazolone was heated with phosphorus penta- and oxychlorides,[2] the 3-methyl group was split off, a Cl attached itself at 4, but again three Cl's entered the benzene nucleus.

Our investigations in this 4-quinazolone group have led to the synthesis and study of derivatives carrying the following substitutions:

1. At position, 2-,methyl, ethyl, normal and isopropyl, isobutyl, isoamyl, phenyl, *m*- and *p*-nitrophenyl, benzyl, *p*-tolyl, COOH, and various complex radicals and residues.

2. At position, 3-,methyl, ethyl, normal and isopropyl, iso- and secondary butyl, isoamyl, allyl, phenyl, *o*-tolyl, *p*-anisyl, benzyl, beta-naphthyl, CH_2COOR, CH_2CONH_2, CH_2CN, C_6H_4COOR, $C_6H_4CONH_2$, C_6H_4CN, the amino group and its derivatives, quinazolonyls, and dimethyl dicarbethoxypyrrole.

3. At position, 4-,OH, Cl, and OR.

4. On the benzene nucleus-,alkyls, halogens, nitro, amino (and derivatives), and COOH.

In the various series, where homologs of analogous structure are compared, it will be found that the melting point falls quite steadily with rise in molecular weight, the iso compounds melting higher than the isomers carrying normal alkyls. This is perhaps not so surprising since many series of anthranilic compounds (for example, the alkyl and acylamino anthranilic acids, the acylanthranilic nitriles, etc.) exhibit a similar behavior.

In addition to the 4-quinazolones, our studies have included also the 2-quinazolones (2-hydroxyquinazolines), 2,4-dihydroxyquinazolines (2,4-

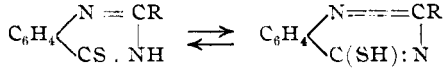
[1] Bogert and May, *Loc. cit.*

[2] Compare Fischer, *Ber.*, **32**, 1297 (1899).

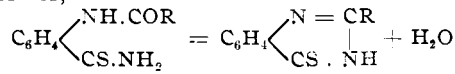
diketotetrahydroquinazolines, or benzoylene ureas), and a few other types.

B. Thioquinazolines.

The work in the domain of the oxygenated quinazolines led quite naturally to the production of bodies of analogous structure carrying sulphur instead of oxygen, and known as the 4-thioquinazolone or quinazolthion (4) type,[1]

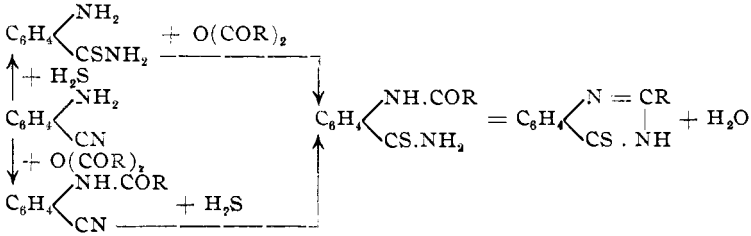


Since anthranilamides, as noted, easily condense to quinazolines by loss of water, it seemed probable that the corresponding thioamides would yield thioquinazolines,



and the results corroborated this fully.

The acylanthranilic thiamide was prepared either by first converting the anthranilic nitrile to the amide by the direct addition of hydrogen sulphide and then acylating, or by first acylating and then adding the H_2S:



By the use of thiol acids (for example, thioacetic acid) in sealed tubes, the thioquinazoline was obtained direct. The thiol acid first acylates the amino group. The by-product of this acylation, H_2S, cannot escape from the tube and is thus forced to attach itself to the CN, thereby changing it to the thioamide. The acylaminothioamide then passes to the thioquinazoline by loss of water.

As comparatively few thiol acids are readily available, we made our reaction more widely applicable by substituting the acid anhydride with sodium sulphide for the thiol acid. Thus, when anthranilic nitrile is heated with acetic anhydride and sodium sulphide in open flasks or, better, in sealed tubes, the anhydride first acetylates the amino group with formation of acetic acid as the by-product. The latter then attacks the sodium sulphide, setting free hydrogen sulphide and forming sodium acetate. The hydrogen sulphide converts the acetoanthranilic nitrile to the thioamide, which then splits out water and gives the quinazoline, the sodium acetate possibly assisting in the elimination of this molecule of water.

These thioquinazolines crystallize in beautiful yellow needles or prisms when alcohol is used as the solvent. By virtue of the —CS.NH— $\rightleftarrows$ —C(SH) : N— group, they dissolve freely in solutions of the caustic

[1] Bogert, Breneman and Hand, THIS JOURNAL, 25, 372 (1903); Bogert and Hand, *Ibid.*, 25, 935 (1903).

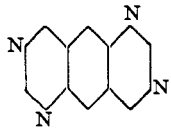
alkalies and are reprecipitated therefrom by carbon dioxide or by acetic acid.

Like the corresponding oxygen compounds, the melting point of the 2-alkyl derivatives steadily falls with rise in molecular weight, the iso compounds melting higher than the isomers of normal structure.

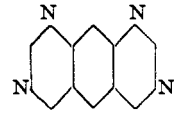
In the course of the investigation, we have used both simple and substituted anthranilic acids.

C. Naphthotetrazines.

Our syntheses of the simple quinazolines having resulted so satisfactorily, we decided to attempt the synthesis of compounds of the following types,



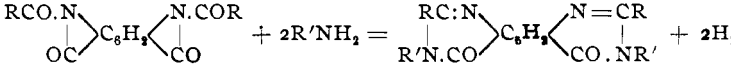
(1,3,6,8-Naphthotetrazine)



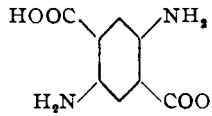
(1,3,7,9-Naphthotetrazine)

and in this were equally fortunate.

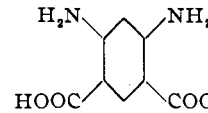
Naphthotetrazines of both types were prepared from the bis-acylanthranils of the appropriate diaminophthalic acid and various primary amines,[1]



as well as from the diaminophthalic acids themselves by reactions similar to those employed for the synthesis of the simple quinazolines. The diaminophthalic acids used, which must be, of course, of anthranilic structure, were



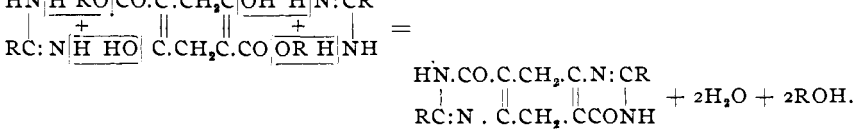
(3,6-Diamino-1,4-phthalic acid)



(4,6-Diamino-1,3-phthalic acid)

These acids, as can be seen by a glance at their graphic formulas, are only double anthranilic acids, and undergo similar reactions, the former yielding the 1,3,6,8-naphthotetrazines, and the latter the 1,3,7,9-isomers.

1,3,6,8-Naphthotetrazines were also obtained by condensing succinylosuccinic esters with amidines:[2]



All of these naphthotetrazine derivatives so far obtained by the above processes are either infusible or melt very high. They are insoluble in the ordinary neutral organic solvents. When they carry the —NH.CO—

[1] Bogert and Nelson, THIS JOURNAL, 29, 729 (1907); Bogert and Kropff, *Ibid.*, 31, 1071 (1910).

[2] Bogert and Dox, *Ibid.*, 27, 1127 and 1302 (1905).

$\rightleftarrows$ —N : C(OH)— group, they dissolve readily in solutions of the caustic alkalies, whence they are reprecipitated by carbon dioxide or by acetic acid.

The naphthotetrazine prepared from guanidine and succinylosuccinic ester gives a sodium salt crystallizing in beautiful yellow needles or prisms which have a magnificent greenish fluorescence.

This, in a very hasty and imperfect way, indicates the main lines along which this particular field of investigation has been developed. It would only weary you to refer even hurriedly to the many subordinate lines of investigation radiating from these main ones, necessitating or resulting in the synthesis of many hundreds of new organic substances. I can only say, as I did at the outset of this address, that it has all been most interesting to us, and that we are still carrying on the work.

The articles published in the progress of these researches are listed below. They have all appeared in *The Journal of the American Chemical Society*, to which the volume numbers refer:

1900 1. A new synthesis in the quinazoline group. M. T. Bogert and A. H. Gotthelf, THIS JOURNAL, **22**, 129.

2. The direct synthesis of ketodihydroquinazolines from orthoamino acids. M. T. Bogert and A. H. Gotthelf, *Ibid.*, **22**, 522.

1901 3. The synthesis of alkyl ketodihydroquinazolines from anthranilic acid. A. H. Gotthelf, *Ibid.*, **23**, 611.

1902 4. The synthesis of alkyl ketodihydroquinazolines from anthranilic nitrile. M. T. Bogert and W. F. Hand, *Ibid.*, **24**, 1031.

1903 5. The synthesis of alkyl thioketodihydroquinazolines from anthranilic nitrile. M. T. Bogert, H. C. Breneman and W. F. Hand, *Ibid.*, **25**, 372.

6. 3,5-Bibrom-2-aminobenzoic acid; its nitrile and the synthesis of quinazolines from the latter. M. T. Bogert and W. F. Hand, *Ibid.*, **25**, 935.

1905 7. The synthesis of 5-nitro-4-ketodihydroquinazolines from 6-nitro-2-aminobenzoic acid, 6-nitro-2-acetylaminobenzoic acid, and from the corresponding nitro acetylanthranil. M. T. Bogert and V. J. Chambers, *Ibid.*, **27**, 649.

8. The condensation of succinylosuccinic acid diethyl ester with guanidine. A derivative of 1,3,5,7-naphthotetrazine, a new heterocycle. M. T. Bogert and A. W. Dox, *Ibid.*, **27**, 1127.

9. Some acyl derivatives of homoanthranilic nitrile, and the 7-methyl-4-ketodihydroquinazolines prepared therefrom. M. T. Bogert and A. Hoffman, *Ibid.*, **27**, 1293.

10. The condensation of succinylosuccinic acid diethyl ester with acetamidine: 2,6-dimethyl-4,8-dihydroxy-9,10-dihydro-1,3,5,7-naphthotetrazine. M. T. Bogert and A. W. Dox, *Ibid.*, **27**, 1302.

11. The synthesis of 2-methyl-5-nitro-4-ketodihydroquinazolines from 6-nitro acetanthranil and primary amines. M. T. Bogert and H. A. Seil, *Ibid.*, **27**, 1305.

12. The synthesis of 7-nitro-2-alkyl-4-ketodihydroquinazolines from 4-nitro acetanthranilic acid and from 4-nitro acetanthranil. M. T. Bogert and S. H. Steiner, *Ibid.*, **27**, 1327.

13. 5-Brom-2-aminobenzoic acid and some of its derivatives. M. T. Bogert and W. F. Hand, *Ibid.*, **27**, 1476.

1906 14. The preparation of 6-brom-4-ketodihydroquinazolines from 5-brom-2-aminobenzoic acid and certain of its derivatives. M. T. Bogert and W. F. Hand, *Ibid.*, **28**, 94.

15. On 5-amino-4-ketodihydroquinazolines and 5-amino-2-methyl-4-ketodihydroquinazolines. M. T. Bogert and V. J. Chambers, *Ibid.*, **28**, 207.

16. On the condensation of succinylosuccinic esters with amidines. M. T. Bogert and A. W. Dox, *Ibid.*, **28**, 398.

17. On a 3-aminoquinazoline and the corresponding 3,3′-diquinazolyl, from 6-nitro acetanthranil and hydrazine hydrate. M. T. Bogert and H. A. Seil, *Ibid.*, **28**, 884.

18. Synthesis of 6-nitro-2-methyl-4-ketodihydroquinazolines from 5-nitro acetanthranil and primary amines. M. T. Bogert and E. P. Cook, *Ibid.*, **28**, 1449.

1907 19. The synthesis of quinazoline carboxylic acids from 4-aminoisophthalic acid and from aminoterephthalic acid. M. T. Bogert, J. D. Wiggin and J. E. Sinclair, *Ibid.*, **29**, 82.

20. A strange case of poisoning. M. T. Bogert, *Ibid.*, **29**, 239.

21. On 2,3-dialkyl-4-quinazolones and the products obtained by alkylating 2-alkyl-4-quinazolones (2-alkyl-4-hydroxyquinazolines). M. T. Bogert and H. A. Seil, *Ibid.*, **29**, 517.

22. The synthesis of 1,3,6,8-naphthotetrazines from paradiaminoterephthalic acid and from certain of its derivatives. M. T. Bogert and J. M. Nelson, *Ibid.*, **29**, 729.

1908 23. On certain 7-nitro-2-methyl-4-quinazolones from 4-nitroacetanthranil. M. T. Bogert and W. Klaber, *Ibid.*, **30**, 807.

1909 24. 3-Amino-*o*-phthalic acid and certain of its derivatives. M. T. Bogert and F. L. Jouard, *Ibid.*, **31**, 483.

25. On certain quinazoline oxygen ethers of the type —N:C(OR)— and the isomeric —NR.CO— compounds. M. T. Bogert and C. E. May, *Ibid.*, **31**, 507.

26. On some amino and nitroamino derivatives of benzoic, metatoluic and metaphthalic acids. M. T. Bogert and A. H. Kropff, *Ibid.*, **31**, 841.

27. On 2-methyl-3-amino-4-quinazolone and certain of its derivatives. M. T. Bogert and R. A. Gortner, *Ibid.*, **31**, 943.

28. On 6-methyl-7-aminoquinazolones, 7-nitroquinazolone-6-carboxylic acids, and 1,3,7,9-naphthotetrazines. M. T. Bogert and A. H. Kropff, *Ibid.*, **31**, 1071.

1910 29. On oxalyl anthranilic compounds and quinazolines derived therefrom. M. T. Bogert and R. A. Gortner, *Ibid.*, **32**, 119.

HAVEMEYER LABORATORIES, COLUMBIA UNIVERSITY,
March 28, 1910.

THE CAUSE OF COLOR IN ORGANIC COMPOUNDS.[1]

BY RICHARD SYDNEY CURTISS.

Received April 16, 1910.

During an investigation in the mesoxalic ester series, I have been led to a study of the causes which underlie the phenomenon of color in some of these very simple aliphatic compounds.[2] In doing so I have found the subject fascinating, and it has seemed to me that it might be of interest to a general audience, in which I assume the great majority are not organic chemists. I shall try to present some of the simpler facts and theories on which our ideas of color cause rest.

[1] Address of the Chairman of the Division of Organic Chemistry of the American Chemical Society delivered in general session of the Society at Harvard University, December 29, 1909.

[2] Curtiss and Spencer, THIS JOURNAL, **31**, 1033; Curtiss, *Am. Chem. J.*, **35**, 477.