

oxidation, may reasonably lead to the assumption that it is either coniine or, possibly, a mixture of bases such as is obtained in a similar manner from *Conium maculatum*.

The fact that the proportion of alkaloid found by us in the *Aethusa* was so very small, and that the plant apparently contains no other substance to which a toxic action can be attributed, would seem to afford some justification for the conclusion of Dr. Harley¹ that it is free from the noxious properties which it has been stated to possess. It is quite possible, however, that this conclusion, based upon the results of physiological experiments with the expressed juice of the plant, may only be correct within certain limitations. It has been observed, for example, in the case of *Conium*, that the plant varies in narcotic power according to the stage of its development, and to the weather and climate, being most active when the fruit is still green, in hot and dry seasons, and in warm countries.²

Notwithstanding the contradictory nature of the statements that have been recorded respecting the properties of the *Aethusa*, and whatever may be the explanation of these discrepancies, there remains the important and positive fact that, in accordance with the observations of earlier investigators, the plant examined by us contained a small amount of a volatile alkaloid resembling coniine in its physical and chemical characters, and, as we have shown, also in its physiological action. In view of this fact, it can not be considered improbable that, under favorable conditions of growth, the proportion of alkaloid may be increased to such an extent as to impart to the plant the poisonous properties ascribed to it.

5-BROM-2-AMINO BENZOIC ACID AND SOME OF ITS DERIVATIVES.³

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5-BROMACETANTHRANILIC acid was prepared by the direct bromination of acetanthranilic acid, and also by the oxidation of 5-brom-*o*-acettoluide. Alt⁴ proved that these two methods gave

¹ *Loc. cit.*

² Compare Farr and Wright: *Pharm. Journ.* [4], 18, 185; "United States Dispensatory," Eighteenth Edition, p. 447, also Millsbaugh: *Loc. cit.*

³ Read at the Buffalo Meeting of the American Chemical Society, June 22, 1905.

⁴ *Ber.*, 22, 1643 (1889).

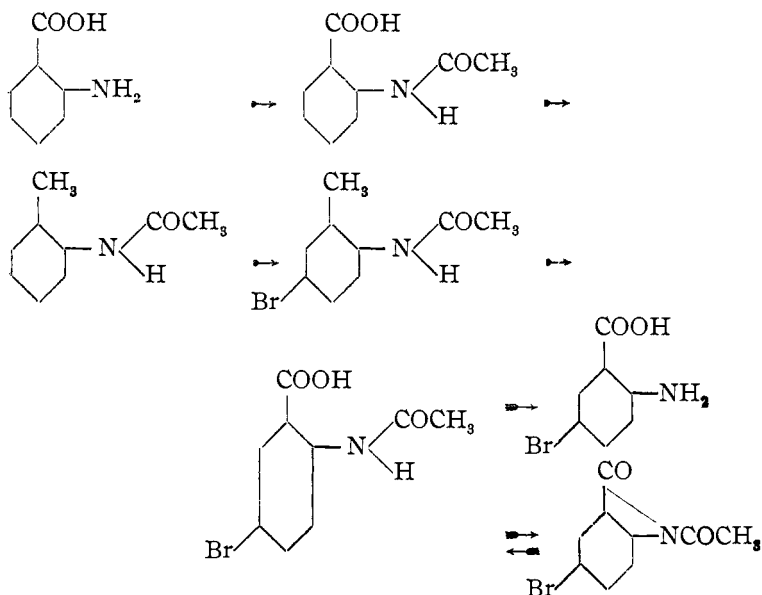
exactly the same product, and our own results confirm this fully. From the bromacetanthranilic acid, the bromanthranilic acid was obtained by saponifying with concentrated hydrochloric acid.

A great deal of time was spent in studying the barium salts of these two acids. The barium salt of the acetyl acid crystallizes in two forms, one approximately anhydrous, and the other carrying three and a half or four molecules of water, while that of the unacetylated acid crystallizes approximately anhydrous. In both cases, however, the analytical figures for barium were uniformly low. It seemed impossible to free these salts of all moisture below the point at which they decompose. Alt¹ mentions a barium salt of 5-bromanthranilic acid which crystallized with four molecules of water. This salt we did not encounter, possibly because our salt was prepared in a different way.

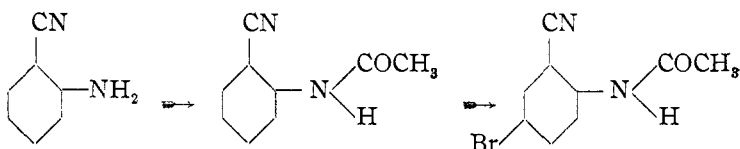
By treating the bromacetanthranilic acid with acetic anhydride, the corresponding bromacetanthranil was obtained.

We also prepared the bromacetanthranilic nitrile by direct bromination of acetanthranilic nitrile.

These various lines of work may be represented thus:



¹ *Loc. cit.*



Quinazolines were prepared from the bromanthranilic acid, its acetyl derivative, the bromacetanthranil, and from the bromacetanthranilic nitrile. These quinazolines will be described in a subsequent paper.

The authors wish to express their indebtedness to Messrs. H. J. Smith and J. E. Jacob, of the Chemical Laboratory of the Mississippi Agricultural and Mechanical College, by whom most of the analytical work required in this investigation was performed, and without whose willing and efficient coöperation the publication of this research would have been greatly delayed.

EXPERIMENTAL.

Acetanthranilic Acid.

Acetanthranilic acid, (1) $\text{HOOC.C}_6\text{H}_4.\text{NHCOCH}_3$ (2), was prepared according to the method of Jackson,¹ by the action of acetic anhydride upon anthranilic acid. A very good solvent for recrystallizing the crude product is 50 per cent. acetic acid. The pure acid is more or less difficultly soluble in cold water, toluene, carbon tetrachloride, chloroform, carbon disulphide, ether, cold aniline, cold dilute alcohol, or cold 50 per cent. acetic acid; moderately soluble in cold glacial acetic acid, cold 95 per cent. alcohol, or hot dilute alcohol; easily soluble in hot glacial or 50 per cent. acetic acid, hot 95 per cent. alcohol, hot aniline, or in acetone.

5-Bromacetanthranilic Acid.

5-Bromacetanthranilic acid, $\text{C}_6\text{H}_3(\text{COOH})(\text{NHCOCH}_3)(\text{Br})$ (1,2,5), was prepared (I) by the direct bromination of acetanthranilic acid, (II) by the oxidation of 5-brom-*o*-acettoluide, and (III) by the hydrolysis of 5-bromacetanthranil.

(I) *Preparation of 5-Bromacetanthranilic Acid by Brominating Acetanthranilic Acid.*—For satisfactory bromination the acetanthranilic acid must be in a very fine state of division; no lumps can be used.

The finely powdered acetanthranilic acid was placed in a round-bottomed flask, sufficient water added to form a thin paste, and a

¹ *Ber.*, 14, 886 (1881).

solution of slightly more than the calculated amount of bromine dissolved in aqueous potassium bromide solution added gradually with shaking. The bromine was readily absorbed, and if the mixture was sufficiently dilute the temperature did not rise very rapidly. The addition of the bromine was continued until a yellow color was obtained that did not fade appreciably after standing for at least half an hour. The substitution was then complete. One hundred grams of acetanthranilic acid were thus brominated in the course of an hour. The product was very flocculent, and much more bulky than the original acetanthranilic acid. The thick mass was poured into a large porcelain dish, allowed to stand about twelve hours, filtered on a large Buchner funnel, and washed thoroughly. The precipitate was so fine that it clogged the filter and rendered the washing tedious and troublesome. The washed precipitate, when dry, was very light, and nearly colorless. It was dissolved in 95 per cent. alcohol, boiled with bone-black, filtered hot, hot water added to the filtrate to permanent cloud, and the solution allowed to cool. The crystals obtained, recrystallized from 50 per cent. acetic acid, separated in beautiful clear six-sided microscopic prisms, m. p. 218–219° (corr.). By recrystallization from glacial acetic acid, the melting-point was raised to 222–223° (corr.).

(II) *Preparation of 5-Bromacetanthranilic Acid by the Oxidation of 5-Brom-o-acettoluide.*—After experimenting with various methods of brominating *o*-acettoluide, we found that the use of the bromide-bromate mixture was the most satisfactory. The process used was as follows:

Fifty grams of *o*-acettoluide were dissolved in 500 cc. of 95 per cent. alcohol, the solution heated to boiling, a solution of 66.55 grams of potassium bromide in 200 cc. hot water added, the solution heated nearly to boiling, slightly more than sufficient hydrochloric acid added to decompose all potassium bromide, and a hot solution of 18.685 grams of potassium bromate dissolved in the least possible amount of water gradually stirred in. The brominated body separated suddenly. It was redissolved by continuing the heating and adding alcohol, if necessary, to prevent its enclosing unbrominated toluide. If the solution did not show excess of bromine at this point, a little more bromide and bromate were added until excess of bromine was evident. The bromtoluide was precipitated by the addition of a large amount of water, the

mixture cooled thoroughly, the precipitate filtered out, washed thoroughly and dried. It was purified by slow crystallization (on the steam-bath) from dilute alcohol, giving bundles of colorless, silky, microscopic hairs, m. p. 154° (corr.). Niementowski¹ gives the melting-point as $156-157^{\circ}$. As our product was entirely homogeneous and of fine appearance, we did not attempt to raise the melting-point by further recrystallizations, deeming it sufficiently pure for the preparation of the bromoacanthranilic acid. The yield of bromoacetoluide was practically quantitative.

The dry bromoacetoluide is very hard to wet again. We found it necessary to dissolve it in the least possible quantity of boiling acetone and reprecipitate with a large volume of boiling water. A mud-like mass resulted, which was readily oxidized by potassium permanganate.²

Fifty grams of the dry toluide were changed to this mud, and suspended in four liters of boiling water. The acetone was boiled out, and finely pulverized permanganate added gradually. The amount of permanganate required was between 300 and 400 grams. The mixture was kept boiling vigorously, and when once well under way the oxidation proceeded quite rapidly, and was complete in about two hours and a half. A test portion filtered off and cooled deposited no unchanged toluide, and the permanganate color was not discharged by further boiling. The excess of permanganate was then destroyed by adding alcohol, and the whole was filtered hot. The filtrate was allowed to stand about twelve hours, and in case any unoxidized toluide separated it was removed by filtration. The filtrate was acidified with hydrochloric acid (acetic acid does not transpose the salts of the acetamino acid, although it readily transposes those of the unacetylated acid), the precipitate washed well with water, treated with bone-black, and crystallized from toluene. Short, thick, small prisms were obtained, melting at $223-224^{\circ}$ (corr.), identical with the bromoacanthranilic acid obtained by the direct bromination of acetanthranilic acid. The yield was good.

(III) *Preparation of 5-Bromoacanthranilic Acid by the Hydrolysis of 5-Bromoacanthranil.*—5-Bromoacanthranil was boiled with water, the precipitate filtered out, dried, and recrystallized from toluene. Small, clear, microscopic prisms resulted, m. p.

¹ Ber., **25**, 863 (1892).

² Alt: *Loc. cit.*

221–222° (corr.), identical with the bromacetanthranilic acid prepared by the above two methods.

The pure 5-bromacetanthranilic acid forms crystals which appear under the microscope as beautiful, glassy, six-sided prisms. The melting-point of these crystals varies greatly according to the rapidity with which they are heated, as both Jackson¹ and Alt¹ observed. By rapid heating we have obtained as high a melting-point as 223–224° (corr.). The acid is difficultly soluble in water, carbon tetrachloride, chloroform, carbon disulphide, ligroin, 50 per cent. acetic acid, toluene, cold aniline, or cold dilute alcohol; moderately soluble in cold acetone, cold glacial acetic acid, cold 95 per cent. alcohol, or hot dilute alcohol; easily soluble in ether, hot aniline, hot glacial acetic acid, hot acetone, or hot 95 per cent. alcohol. It dissolves instantly and completely in solutions of the caustic alkalies or of ammonia. It decomposes alkaline carbonates or magnesium carbonate readily, but barium carbonate very slowly, the barium salt being very difficultly soluble. It is easily saponified by hot concentrated hydrochloric acid. Its salts are not transposed by acetic acid.

The acid was burned with the DeRoode mixture in a long combustion tube, and gave the following results: Found: C, 41.86; H, 3.26; Br, 31.03. Calculated for $C_9H_8O_3NBr$: C, 41.87; H, 3.10; Br, 31.00.

Barium Salt of 5-Bromacetanthranilic Acid.—The first experiments were conducted with bromacetanthranilic acid obtained by the bromination of acetanthranilic acid. These experiments were then repeated with bromacetanthranilic acid from bromacettoluide. The crystals obtained from the two series appeared identical under the microscope.

The bromacetanthranilic acid was boiled with excess of dilute barium hydroxide solution, the excess of barium precipitated by a stream of carbon dioxide, and the mixture filtered hot. On cooling, there first separated a mixture of transparent, microscopic, needle-like prisms, with a few larger, six-sided, transparent prisms. By filtering off the first crop of crystals, other crops separated from the mother-liquor containing less and less of the microscopic needles and more and more of the larger prisms. The larger prisms were finally obtained apparently free from the needles, but we were not able to secure any first crop crystals

¹ *Loc. cit.*

consisting exclusively of the microscopic needles. The two crystalline forms are easily distinguishable under the microscope. A great many analyses were carried out on the various crops of barium salt, but the results were not very satisfactory. We are of the opinion, as the result of these analyses, that the microscopic needles which separate first are anhydrous, while the larger prisms carry three and a half or four molecules of water. It is difficult to remove all the water from the hydrated crystals below the temperature at which the salt itself is decomposed. The barium salt is very difficultly soluble in water even at its boiling-point.

5-Bromanthranilic Acid.

This was prepared by saponifying 5-bromacetanthranilic acid with boiling concentrated hydrochloric acid. The bromacetanthranilic acid used was prepared both from acetanthranilic acid and from the bromacetoluide. Both products gave one and the same bromanthranilic acid, as Alt¹ showed some time ago.

One hundred grams of 5-bromacetanthranilic acid were placed in a two liter round-bottomed flask, and boiled for three hours under a return condenser with 800 cc. of concentrated hydrochloric acid. The hydrochloride of the amino acid is difficultly soluble in concentrated hydrochloric acid. During the boiling a stream of dry hydrogen chloride is passed through the solution. This diminishes the bumping which generally occurs, and keeps the solution saturated with hydrochloric acid gas, so that on cooling with ice practically all of the hydrochloride of the amino acid is precipitated. This precipitate is filtered out, washed with cold, concentrated hydrochloric acid, sucked dry on the pump, and transferred to a large porcelain dish. It is then covered with fifteen volumes of cold water, cracked ice is added, and most of the hydrochloric acid is neutralized with ammonia. It is not advisable to attempt to neutralize the hydrochloric acid completely, as the hydrochloride is completely dissociated by the large volume of water added. The free amino acid is filtered out, washed thoroughly with ice water, recrystallized and treated with boneblack. Toluene proved a very satisfactory menstruum for crystallization of the substance.

5-Bromanthranilic acid forms colorless crystals. When rapidly heated, they melt at 219–220° (corr.), with previous softening. Alt¹ gives the melting-point as 211.5–212°. The acid is insoluble

¹ *Loc. cit.*

or difficultly soluble in water, benzene, toluene, xylene, ligroin, oil of turpentine, carbon tetrachloride, carbon disulphide, ethyl acetate, cold chloroform, or cold dilute alcohol; moderately soluble in hot chloroform, in dry ether, or cold acetone; easily soluble in hot acetone, in hot dilute alcohol, in 95 per cent. alcohol, or in aniline. The copper salt is apple-green, as Alt¹ states, and not bright blue as reported by Hübner and Petermann.²

Some of the acid was purified through its barium salt. In decomposing the solution of the barium salt with hydrochloric acid, the solution should be cold and the acid added gradually, or the amino acid may precipitate in a gummy condition difficult to filter and wash. An excess of hydrochloric acid does no harm, as the hydrochloride is immediately dissociated by the excess of water.

Analysis of the purified acid gave the following results: Found: C, 38.32; H, 2.72; Br, 37.55. Calculated for $C_7H_6O_2NBr$: C, 38.89; H, 2.73; Br, 37.02.

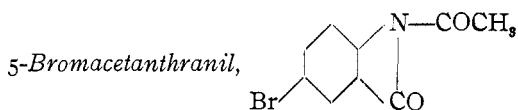
Hydrochloride of 5-Bromanthranilic Acid.—Dry hydrogen chloride was passed through a warm solution of the acid in absolute ether. The precipitated hydrochloride was filtered out and dried. It is rapidly decomposed by moisture. A small amount, washed a few times with cold water on a filter, and the residue then dissolved in nitric acid, gave no reaction at all for chlorine ions. The salt gives off hydrochloric acid quite rapidly even in the air.

Barium Salt of 5-Bromanthranilic Acid.—The purified acid was suspended in boiling water, dilute barium hydroxide solution added to slightly alkaline reaction and the boiling continued for some time, adding more baryta water, if necessary. The excess of barium was precipitated by carbon dioxide, the solution filtered boiling hot, and allowed to cool slowly. Transparent, six-sided prisms separated in mossy colonies. These crystals were anhydrous. They darken slightly on standing, are very difficultly soluble in cold water, and only moderately soluble in boiling water.

Alt,¹ by boiling the acid with barium carbonate, obtained a salt carrying four molecules of water. This salt we did not encounter.

¹ *Loc. cit.*

² *Ann. Chem.* (Liebig), 149, 133.



—5-Bromacetanthranilic acid was boiled with an excess of acetic anhydride. The crystals which separated on cooling were filtered out, dried, and recrystallized from carbon tetrachloride.

The pure anthranil crystallizes in colorless scales, m. p. 131° (corr.).

The following figures were obtained on analysis: Found: C, 45.04; H, 2.50; N, 6.24 and 6.16; Br, 33.31. Calculated for $C_9H_6O_2NBr$: C, 45.01; H, 2.13; N, 5.83; Br, 33.32.

5-Bromacetanthranilic Nitrile.

5-Bromacetanthranilic Nitrile, $C_8H_5(CN)(NHCOCH_3)(Br)_{(1,2,5)}$. —Acetanthranilic nitrile (m. p. 132.5° (corr.)) was brominated by suspending it in water and passing in a current of air laden with bromine vapor. Five or six hours were required to complete the bromination. The crude product was filtered out, washed, treated with bone-black, and recrystallized from water. Larger crystals were obtained from carbon tetrachloride. During the bromination the temperature of the liquid must not be permitted to rise above about 30° , or the product may be spoiled.

The pure nitrile forms clear, six-sided prisms, m. p. 158° (corr.); insoluble or difficultly soluble in cold water, carbon disulphide, cold benzene, or cold carbon tetrachloride; moderately soluble in cold dilute alcohol, hot water, cold toluene or hot carbon tetrachloride; easily soluble in 95 per cent. alcohol, hot dilute alcohol, acetone, ethyl acetate, hot benzene, hot toluene, or chloroform.

Bromine found, 33.52; calculated for $C_8H_5ON_2Br$, 33.46.

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ON THE OCCURRENCE OF ARSENIC IN WINES.

BY H. D. GIBBS AND C. C. JAMES.

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WHILE engaged upon the analysis of 100 samples of California dry, red wines, the frequent occurrence of coal-tar dyes induced us to test for arsenic which is often found in certain dyes. We