

at less, neon is remarkably luminescent. The phenomenon is inhibited by the presence of moisture or of CO_2 , but not by hydrogen. After several hours the luminescence diminishes, but is restored by the induction spark.

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ON THE CRYSTALLINE ALKALOID OF CALYCANTHUS GLAUCUS.

THIRD PAPER.—ON ISOCALYCANTHINE, ISOMERIC WITH CALYCANTHINE.¹

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Received September 28, 1909.

In previous papers² I have shown how to extract calycanthine from the seeds of *Calycanthus glaucus* and prepare the usual salts of the alkaloid. It was shown that calycanthine contained half a molecule of water of crystallization which was removable by heating the crystals to 120° for a few hours, that the anhydrous alkaloid was a monacid base having the formula $\text{C}_{11}\text{H}_{14}\text{N}_2$ and that the formulas of all the salts, of which a considerable number were prepared and analyzed, corroborated this formula.

Having exhausted all the material on hand,³ I ordered a new batch of the same seeds from the same dealer and worked them up by exactly the same method as before. But while the seeds of the second batch looked exactly like those of the first batch and the alkaloid itself prepared from the second batch looked exactly like the calycanthine isolated from the first batch, it very soon became evident that the alkaloid from the second batch was not in every respect identical with the one from the first batch. Calycanthine melted, crystalline at $216-18^\circ$ and anhydrous at $243-4^\circ$ and lost its water of crystallization at 120° without otherwise being changed by the heat. The alkaloid of the second batch of seeds melts crystalline at $212-4^\circ$ and its water of crystallization cannot be removed by heat without partial decomposition of the base, as is indicated by its becoming yellowish and then having no definite melting point. That the alkaloid from the second batch also contains water of crystallization is shown by its losing weight when kept *in vacuo* over sulphuric acid or phosphoric anhydride. But the loss of water of crystallization under these conditions, while fast in the beginning, soon becomes so exceptionally slow that, unless a considerable amount of the alkaloid be taken, the loss during 24 hours ceases to be indicated by the balance. I have been drying about 2 grams of the alkaloid *in vacuo* over sulphuric acid for

¹ I wish to express my thanks to Ely Lilly and Company for the special care with which they extracted for me, free of charge, a large quantity of the seeds.

² THIS JOURNAL, 27, 144 and 1418.

³ Having been assured by the dealer of his ability to supply me with all the seeds I might need, I neglected to keep a sample of calycanthine or of its salts for later comparisons.

about nine months, weighing it every month, but so far the weight continues to diminish. Attempts to analyze the alkaloid dried in the air gave discordant results, showing that the base begins losing weight as soon as made. Attempts to dry the alkaloid *in vacuo* over phosphoric anhydride at 130° or in a current of dry hydrogen at 120° also failed to bring the alkaloid to constant weight. When dried *in vacuo* over phosphoric anhydride at 165° the alkaloid begins to sublime.

Having failed to dehydrate the alkaloid by these methods, I have devised a method by which it can be obtained anhydrous in a very short time. For this purpose the pure crystalline alkaloid, obtained by repeated recrystallizations from acetone and water, as described in the first paper, is dissolved in chloroform of which about 20 parts by volume are required for solution. The liquid is turbid and does not become clear even upon addition of considerable quantities of chloroform, showing the turbidity to be due to separation of the water of crystallization. The turbid liquid is shaken with calcined potassium carbonate and the now clear liquid filtered. The solution is kept *in vacuo* over paraffin till the latter absorbs all of the solvent. A crystalline mass is left which is the anhydrous alkaloid. A quicker way is to pass a current of dry hydrogen over the surface of the clear chloroform solution till the volume of the latter is reduced to about one-third, and then add a considerable amount of petroleum ether. On standing over night most of the anhydrous alkaloid crystallizes out in heavy prisms. Analysis of the alkaloid thus obtained gave figures which leave no doubt about its formula being the same as that of anhydrous calycanthine, *i. e.*, $C_{11}H_{14}N_2$. The salts of the alkaloid, of which a considerable number were made and analyzed, also showed that the underlying base had the above formula, though the melting points and the amounts of the water of crystallization of some of these salts differed from the corresponding constants of the corresponding calycanthine salts. Since the anhydrous alkaloid from the second batch of seeds has the same formula as anhydrous calycanthine but has a different melting point and shows different behavior with respect to the removal of the water of crystallization from the hydrated base, the two alkaloids must be isomeric. The alkaloid from the second batch was therefore named *isocalycanthine*. Whether the seeds of the two batches, while looking alike, nevertheless belong to different species of *Calycanthaceae*, or the difference between the alkaloids is due to a difference in the age of the plants, I shall try to determine later. Judging from the crystallographic measurements made by Prof. Kraus, isocalycanthine is identical with the alkaloid Dr. Wiley had in his hands,¹ but since the melting point given by Wiley (219°) is different from that of isocalycanthine (hydrated $212-214^{\circ}$, anhydrous $235-236^{\circ}$) as well as

¹ *Drugg. Circular*, 1896, 55.

from that of calycanthine (hydrated 216–218°, anhydrous 243–244°), I cannot be positive about that.

While the exact amount of water of crystallization in hydrated isocalycanthine has not yet been determined, it is quite probable that the formula of the alkaloid obtained by recrystallization from acetone and water is $C_{11}H_{11}N_2 \cdot \frac{1}{2}H_2O$.

Isocalycanthine as obtained by crystallization from acetone and water is extremely easily soluble in pyridine. It dissolves in about 8 parts of acetone, about 6000 parts of water, about 20 volumes of chloroform giving a turbid solution, about 80 parts cold and about 25 parts hot alcohol. It is difficultly soluble in ether and almost insoluble in benzene. The saturated aqueous solution of isocalycanthine gives no turbidity with Mayer's reagent, unless acid is added; with Wagner's reagent a turbidity appears even in absence of acid. The hydrated alkaloid melts to a yellowish liquid at 212–214°.¹ On prolonged exposure to the air it assumes a yellowish tint. Anhydrous isocalycanthine melts at 235–236° and dissolves in chloroform to a clear solution.

The crystallographic form of hydrated isocalycanthine was determined by Prof. Kraus whose report is here inserted.

Crystallography of Isocalycanthine (EDWARD H. KRAUS).

The crystals of calycanthine which were subjected to a crystallographic examination were obtained by slow crystallization at room temperature from a solution in hot alcohol. They are rather small, the largest being about 2 mm. in length. The crystals are clear, colorless, and transparent and possess high refractive powers. For the most part the crystals are well developed, the faces being bright and affording excellent images.

From the angular measurements of the crystals and the form and position of the etch figures on the basal pinacoid, the crystals must be referred to the orthorhombic bisphenoidal class. Crystals showing the unequal development of $p\{111\}$ and $p'\{1\bar{1}1\}$ were, however, not noted. In general the following forms are to be observed, $p\{111\}$, $p'\{1\bar{1}1\}$, $m\{110\}$, $q\{011\}$, $c\{001\}$, and $a\{100\}$. Of these forms the basal pinacoid, $c\{001\}$, is usually the predominating form, giving the crystals a more or less tabular habit. The forms $p\{111\}$ and $p'\{1\bar{1}1\}$ are, as already said, about equally developed and always give brilliant images. The brachydome, $q\{011\}$, occurs as small narrow faces truncating the edges of the forms $p\{111\}$ and $p'\{1\bar{1}1\}$. The other forms (unit prism, $M\{110\}$, and macropinacoid, $a, \{100\}$) are for the most part small and not always to be observed. Fig. 1 shows the above-mentioned forms in combination. In all, six crystals were measured.

¹ All melting points in this paper were determined in an Anschütz apparatus of about 250 cc. capacity.

In March, 1896, W. H. Melville¹ described the crystallography of some crystals of calycanthine obtained by Professor H. W. Wiley. Although

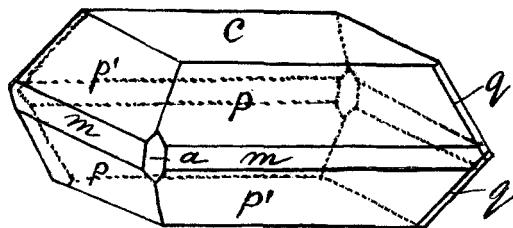


Fig. 1.

Melville's description is not as accurate as it might be, his values obtained for the elements of crystallization are of interest in that they show conclusively that the calycanthine prepared by Wiley and the alkaloid at present under investigation

must, from the standpoint of crystallography, be considered as identical. This is shown clearly by a comparison of the values obtained by Melville and myself.

Crystal system—Orthorhombic.

Crystal class—Bisphenoidal.

AXIAL RATIO $a : b : c = 1.2557 : 1 : 1.3226$ (Krause)

$a : b : c = 1.2490 : 1 : 1.3260$ (Melville).

	Calculated.	Observed.	
		Kraus.	Melville.
$c : p = (001) : (111) =$	$59^{\circ} 24'$	$59^{\circ} 34'$
$c : q = (001) : (011) =$	$52 \quad 54\frac{1}{2}$
$a : m = (100) : (110) =$	$51^{\circ} 28'$	$51 \quad 35\frac{1}{2}$
$p : p' = (111) : (1\bar{1}1) =$	84 39	84 39	84 34
$p : q = (111) : (011) =$	32 25	32 33	32 35

Melville states very distinctly that the development of the crystals did not reveal any of the hemihedral forms of the orthorhombic system which also holds good for these crystals. But since a very large rotation of the plane of vibration was observed by Wiley, it was thought well to determine the symmetry as revealed by the etch figures. Hence, several crystals were etched by allowing cold alcohol to act upon them for a few seconds. The figures obtained on the basal pinacoid clearly showed by their form and position that the crystals must be referred to the orthorhombic bisphenoidal class rather than the orthorhombic bipyramidal as done by Melville. This is in harmony with the rotary properties of the crystals.

The crystals possess a good cleavage parallel to the macropinacoid, a .

The plane of the optical axes is parallel to a .

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Analysis of anhydrous isocalycanthine gave 75.71 per cent. C, 7.64 per cent. H and 15.89 per cent. N. Calculated for $C_{11}H_{14}N_2$, 75.77 per cent. C, 8.12 per cent. H, 16.12 per cent. N. Attempts to determine the molecular

¹ *Druggists' Circular*, March, 1896, 56-57.

weight of anhydrous isocalycanthine by titration with 0.1 *N* hydrochloric acid using hematoxylin as indicator were unsuccessful, the end reaction being very indistinct.

0.4779 gram anhydrous isocalycanthine dissolved in 25 cc. acetone (Merck's from bisulphite and redistilled by myself) gave at 22° in a 200 mm. tube¹ a rotation of 26.685°. Hence $[\alpha]_D^{22} = 697.97^\circ$. It will be seen that isocalycanthine is one of the highest rotating substances known, being, thus far, exceeded only by some members of the santonide group.

The salts of isocalycanthine were almost all made by the same methods as were used for making the salts of calycanthine. While the base underlying them has the same formula as that of the calycanthine salts, many of the isocalycanthine salts differ from the corresponding calycanthine salts in melting points and amounts of water of crystallization. There also seem to be differences in the solubilities between most of the calycanthine and the isocalycanthine salts, but having no more calycanthine or its salts on hand, no exact comparisons could be made in this respect.

Isocalycanthine Hydrochloride, $C_{11}H_{14}N_2 \cdot HCl \cdot H_2O$.—The salt forms heavy colorless cubes. It darkens at 204° and melts to black liquid at 208°. Unlike calycanthine hydrochloride, isocalycanthine hydrochloride is stable in the air, but quickly loses its water of crystallization *in vacuo* over sulphuric acid.

Analysis gave 7.97 and 7.92 per cent. H_2O and 17.01 and 16.90 per cent. Cl (in anhydrous salt). Calculated for $C_{11}H_{14}N_2 \cdot HCl \cdot H_2O$, 7.88 per cent. H_2O and 16.83 per cent. Cl (in anhydrous salt).

The formula of the hydrochloride was further corroborated by titration with 0.1 *N* KOH, using phenolphthalein as indicator:

0.2070 gram of the hydrated salt consumed 8.95 cc. 0.1 *N* KOH and 0.1958 gram consumed 8.72 cc. 0.1 *N* KOH. Calculated for $C_{11}H_{14}N_2 \cdot HCl \cdot H_2O$, 9.01 and 8.53 cc. 0.1 *N* KOH, respectively.

A solution of 0.6755 gram of the anhydrous hydrochloride in 25 cc. water gave at 23° in a 200 mm. tube a rotation of 22.38°. Hence $[\alpha]_D^{23} = 414.14^\circ$.

Isocalycanthine Hydrobromide, $C_{11}H_{14}N_2 \cdot HBr \cdot H_2O$. It forms heavy colorless prisms. When quickly heated the salt darkens at 207° and melts to black liquid at 210–211°. When quickly heated to 190°, then slowly (1° per minute) to 202° and then kept at this temperature for about 4–5 minutes, the salt melts to a black liquid. The hydrated salt is stable in the air, but quickly loses its water of crystallization *in vacuo* over sulphuric acid.

Analysis of the hydrated salt gave 6.38 and 6.42 per cent. H_2O and 29.19 and 29.29 per cent. Br. Calculated for $C_{11}H_{14}N_2 \cdot HBr \cdot H_2O$, 6.59 per cent. H_2O and 29.28 per cent. Br.

A solution of 0.3576 gram of the anhydrous salt in 25 cc. H_2O gave at 19.5° in a 200 mm. tube a rotation of 9.88°. Hence, $[\alpha]_D^{19.5} = 345.36^\circ$.

¹ The apparatus used throughout this work was a J. and J. Fric.

Isocalycanthine Hydriodide, $C_{11}H_{14}N_2.HI.1.5H_2O$.—The salt forms flat needles and contains 1.5 molecules of water of crystallization. (The corresponding calycanthine salt contained no water of crystallization.)

The salt darkens at 211° and melts at 213° to black liquid. It has a very slightly yellowish tint which deepens when the water of crystallization is removed by drying over sulphuric acid.

Analysis gave 8.07 per cent. H_2O and 41.99 and 41.82 per cent. I (in anhydrous salt). Calculated for $C_{11}H_{14}N_2.HI.1.5H_2O$, 8.22 per cent. H_2O and 41.99 per cent. I (in anhydrous salt).

A solution containing 0.3591 gram of the anhydrous salt in 50 cc. of water gave at 24° in a 200 mm. tube a rotation of 4.32° . Hence, $[\alpha]_D^{24} = 300.75^\circ$.

Isocalycanthine Chloroplatinate, $(C_{11}H_{14}N_2)_2.H_2PtCl_6.2H_2O$.—The salt forms thick yellow rods and is considerably lighter in color than the corresponding calycanthine salt (of which I have a very small quantity). The salt turns brown at about 213° and then gradually becomes darker and darker, but does not seem to melt even at 310° . One of the two molecules of water of crystallization goes away when the salt is kept *in vacuo* over sulphuric acid or is heated to 110° for five hours; the other goes away only at 150° within 3–4 hours. On prolonged keeping at this temperature the salt begins to decompose. With the loss of the water of crystallization the yellow color changes to brown.

The salt kept at 110° or over sulphuric acid lost 2.35 per cent. H_2O . Calculated for $(C_{11}H_{14}N_2).H_2PtCl_6.H_2O$, 2.27 per cent. H_2O for one molecule H_2O . At 150° it lost 4.48 per cent. H_2O . Calculated for both molecules of H_2O , 4.54 per cent. H_2O . Analysis gave 24.63 and 24.63 per cent. Pt and 26.69 and 26.76 per cent. Cl. Calculated for $(C_{11}H_{14}N_2)_2.H_2PtCl_6.2H_2O$, 24.54 per cent. Pt and 26.79 per cent. Cl.

Isocalycanthine Chloraurate, $3(C_{11}H_{14}N_2.HAuCl_4) + 2(C_{11}H_{14}N_2.HCl) + 2H_2O$.—At 186.5° the salt darkens and becomes pasty and then does not change even at 260° . It forms brown needles. Dried over sulphuric acid it lost 1.97 and 1.90 per cent. H_2O . Calculated for above formula, 1.80 per cent. H_2O .

Analysis gave 29.02 and 29.14 per cent. Au, and 24.24 and 24.70 per cent. Cl. Calculated for above formula, 29.59 per cent. Au and 24.82 per cent. Cl.

On dissolving the chloraurate in alcohol and adding ether to the solution the salt is decomposed and isocalycanthine hydrochloride crystallizes out. Calycanthine chloraurate behaved in the same way.

Isocalycanthine Nitrate, $C_{11}H_{14}N_2.HNO_3$.—The salt is best made as follows: Dissolve 5 grams air-dried isocalycanthine in 40 cc. water containing a slight excess of acetic acid and add to the solution 6 grams potassium nitrate dissolved in 30 cc. water. On standing over night most of the nitrate crystallizes out in colorless heavy plates. Wash the crystals with as little as possible of cold water and dry over sulphuric acid. When heated in an open capillary tube the salt turns brown on the surface at 183.5° . On further heating the yellow color gradually

spreads downwards, till at 189° the whole is turned to a dark pasty mass. In a vacuum capillary the whole mass turns yellow at 184.5° and melts at $192-194^{\circ}$ to a reddish liquid.

Analysis gave 55.35 per cent. C and 6.37 per cent. H. Calculated for $C_{11}H_{14}N_2$, HNO_3 , 55.66 per cent. C and 6.38 per cent. H.

0.1589 gram gave 25.5 cc. N at 23° and 750 mm. Calculated for above formula 17.72 N. Found, 17.75 N.

A solution of 0.3043 gram in 100 cc. water gave at 20° in a 200 mm. tube a rotation of 2.27° . Hence, $[\alpha]_D^{20} = 372.99^{\circ}$.

Isocalycanthine Acid Sulphate, $C_{11}H_{14}N_2 \cdot H_2SO_4 \cdot 1.5H_2O$.—The hydrated salt forms needles grouped in rosettes and melts, not sharply, at $186-187^{\circ}$. The anhydrous salt becomes dark and pasty at $185-186^{\circ}$. The anhydrous acid sulphate is white. The corresponding calycanthine salt turned yellowish upon loss of the water of crystallization and behaved in an entirely different way upon heating.

Dried over sulphuric acid the salt lost 9.17 and 8.93 per cent. H_2O . Calculated for above formula, 9.03 per cent. H_2O .

Analysis gave 10.75 and 10.77 per cent. S. Calculated for $C_{11}H_{14}N_2 \cdot H_2SO_4 \cdot 1.5H_2O$, 10.71 per cent. H_2O .

A solution containing 0.4239 gram of the hydrated salt in 25 cc. H_2O gave at 27° in a 200 mm. tube a rotation of 9.81° . Hence, $[\alpha]_D^{27} = 289.28^{\circ}$.

Isocalycanthine Neutral Sulphate ($C_{11}H_{14}N_2$) $_2H_2SO_4$.—The salt forms very fine needles, begins to darken at about 208° and melts to thick black liquid at $218-219^{\circ}$.

Analysis gave 6.56 and 6.56 per cent. S. Calculated for above formula, 7.15 per cent. S.

A solution containing 0.1943 gram in 25.5 cc. water gave at 26.5° in a 200 mm. tube a rotation of 5.5° . Hence $[\alpha]_D^{26} = 360.89^{\circ}$.

Like calycanthine, isocalycanthine seems to contain a CH_3N group, though the results obtained by Herzig and Meyer's method were far below the theoretical (calculated 8.63, found 5.28 per cent. CH_3). This may be due to a wandering of the CH_3 into the ring.

Isocalycanthine Picrate, $C_{11}H_{14}N_2 \cdot C_6H_2(NO_2)_3OH \cdot 3/4H_2O$. The salt forms long yellow silky needles, and melts at $175-180^{\circ}$. It lost over sulphuric acid 3.06 per cent. H_2O . Calculated for above formula, 3.22 per cent. H_2O .

0.1472 gram gave 21.6 cc. N at 22° and 746 mm. Calculated for above formula, 16.81 per cent. N. Found, 16.74 per cent. N.

Isocalycanthine Picrolonate, $C_{11}H_{14}N_2 \cdot C_{10}H_8N_4O_5$.—After repeated trials the following method was found to be the best for making this very pretty salt: Dissolve 1 gram isocalycanthine in 20 cc. cold alcohol previously mixed with 1.5 cc. acetic acid (36 per cent.). Add to the solution first a filtered solution of 1 gram picrolonic acid in about 100 cc. cold alcohol and then water to strong turbidity. Heat the liquid till it becomes clear and set aside over night. The picrolonate crystallizes out

in shining, yellowish brown, silky needles. It is almost completely insoluble in water, but easily dissolves in alcohol. It melts at 200° to a greenish black liquid.

0.1889 gram gave 32.1 cc. N at 22° and 741 mm. Calculated for above formula, 18.75 per cent. N. Found, 18.67 per cent. N.

Isocalycanthine Nitrosamine, $C_{11}H_{13}N_2.NO$.—Like calycanthine, isocalycanthine contains an NH group, as it forms an insoluble nitrosamine when its hydrochloride is treated with sodium nitrite, but while calycanthine nitrosamine could be obtained in crystalline condition, the isocalycanthine compound could not be made to crystallize. It was purified by dissolving in pyridine and throwing the solution into much cold water.

It forms a yellowish amorphous powder, darkens at 99° and melts at $106-7^{\circ}$.

0.1597 gram gave 29.6 cc. N at 20° and 754 mm. Calculated for above formula, 20.72 per cent. N. Found, 20.93 per cent. N.

As a secondary base isocalycanthine ought to form a benzoyl and an acetyl compound. All methods so far tried failed to produce such compounds. Either the alkaloid did not react at all, or when higher temperatures were used, it completely resinified.

When digested with acetyl chloride in the cold for a few weeks a hydrochloride of a fine steel-blue color is produced. When heated with acetyl chloride in a sealed tube for 6 hours, a hydrochloride of a dark brown color is formed. With methyl iodide the alkaloid forms the hydriodide of the unchanged base together with two other compounds neither of which seems to have the composition of either the hydriodide of the tertiary base or the iodide of the quaternary base derived from isocalycanthine. I shall try to determine the nature of all these substances and report on them in my next paper. Digested with concentrated sulphuric acid isocalycanthine seems to form a sulphonic acid which is under investigation. The work is continued.

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STUDIES IN NITRATION, VI. NITRANILINE DERIVATIVES OF ORGANIC ACIDS.¹

BY J. BISHOP TINGLE AND C. E. BURKE.

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Bishop Tingle and F. C. Blanck have described a large number of substances which they obtained by the action of nitrating agents on a

¹ Previous papers have appeared as follows: Bishop Tingle and Blanck, *Am. Chem. J.*, **36**, 605 (1906); Bishop Tingle and Rolker, *THIS JOURNAL*, **30**, 822; Bishop Tingle and Blanck, *Ibid.*, **30**, 1395, 1587 (1908); Bishop Tingle and Rolker, *Ibid.*, **30**, 1764 (1908).